

=> file medline

FILE 'MEDLINE' ENTERED AT 16:38:41 ON 28 APR 2006

FILE LAST UPDATED: 27 APR 2006 (20060427/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).  
See also:

<http://www.nlm.nih.gov/mesh/>  
[http://www.nlm.nih.gov/pubs/techbull/nd04/nd04\\_mesh.html](http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html)  
[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_med\\_data\\_changes.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html)  
[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_2006\\_MeSH.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html)

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que 127

```
L16      1164 SEA FILE=MEDLINE ABB=ON  PLU=ON  ("FUJII S"/AU OR "FUJII
          SEISHIRO"/AU)
L17      26 SEA FILE=MEDLINE ABB=ON  PLU=ON  ("DOTTO P"/AU OR "DOTTO
          PAOLO"/AU)
L18      200 SEA FILE=MEDLINE ABB=ON  PLU=ON  ("HAN R"/AU OR "HAN R C"/AU
          OR "HAN R F"/AU OR "HAN R J"/AU OR "HAN R K"/AU OR "HAN R
          L"/AU OR "HAN R N"/AU OR "HAN R O"/AU OR "HAN R S"/AU OR "HAN
          R X"/AU OR "HAN R Y"/AU OR "HAN R Z"/AU OR "HAN RONG"/AU OR
          "HAN RONG BIN"/AU)
L19      26 SEA FILE=MEDLINE ABB=ON  PLU=ON  ("BRISSETTE J"/AU OR "BRISSETT
          E J L"/AU OR "BRISSETTE JANICE L"/AU)
L20      2050 SEA FILE=MEDLINE ABB=ON  PLU=ON  RHO GTP-BINDING PROTEINS/CT
L21      171376 SEA FILE=MEDLINE ABB=ON  PLU=ON  SIGNAL TRANSDUCTION+NT/CT
L22      1597 SEA FILE=MEDLINE ABB=ON  PLU=ON  INTRACELLULAR SIGNALING
          PEPTIDES AND PROTEINS/CT
L23      27550 SEA FILE=MEDLINE ABB=ON  PLU=ON  (P21 OR P(2A)21 OR P21
          PROTEIN KINASE OR P21 SIGNAL TRANSDUCT?)
L24      2229 SEA FILE=MEDLINE ABB=ON  PLU=ON  SKIN AGING/CT
L26      2182 SEA FILE=MEDLINE ABB=ON  PLU=ON  (WRINKL? OR SKIN WRINKL? OR
          WRINK? REDUC?)
L27      0 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L16 OR L17 OR L18 OR L19)
          AND (L20 OR L21 OR L22 OR L23) AND (L24 OR L26)
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=> s 127

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L103      0 (L16 OR L17 OR L18 OR L19) AND (L20 OR L21 OR L22 OR L23) AND
          (L24 OR L26)
```

=> file wpix

FILE 'WPIX' ENTERED AT 16:38:44 ON 28 APR 2006  
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FILE LAST UPDATED: 26 APR 2006 <20060426/UP>  
MOST RECENT DERWENT UPDATE: 200627 <200627/DW>  
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,  
PLEASE VISIT:  
[http://www.stn-international.de/training\\_center/patents/stn\\_guide.pdf](http://www.stn-international.de/training_center/patents/stn_guide.pdf) <

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE  
<http://scientific.thomson.com/support/patents/coverage/latestupdates/>

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE  
[http://www.stn-international.de/stndatabases/details/ipc\\_reform.html](http://www.stn-international.de/stndatabases/details/ipc_reform.html) and  
<http://scientific.thomson.com/media/scpdf/ipcrdwpf.pdf> <<<

>>> UPCOMING NEW DWPI: EFFECTS ON SCRIPT RUNS - SEE NEWS MESSAGE <<<  
'BIX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

=> d que 185

L77 766 SEA FILE=WPIX ABB=ON PLU=ON ("FUJII S"/AU OR "FUJII S I  
C"/AU OR "FUJII S K"/AU OR "FUJII S N"/AU)  
L78 3 SEA FILE=WPIX ABB=ON PLU=ON ("DOTTO G P"/AU OR "DOTTO P"/AU)  
L79 118 SEA FILE=WPIX ABB=ON PLU=ON ("HAN R"/AU OR "HAN R A"/AU OR  
"HAN R G"/AU OR "HAN R H"/AU OR "HAN R J L"/AU OR "HAN R L"/AU  
OR "HAN R S"/AU OR "HAN R Y"/AU)  
L80 6 SEA FILE=WPIX ABB=ON PLU=ON ("BRISSETTE J"/AU OR "BRISSETTE  
J E"/AU OR "BRISSETTE J W"/AU)  
L81 16 SEA FILE=WPIX ABB=ON PLU=ON P21/BIX (L) SIGNAL TRANSDUCT?/BIX  
L82 39 SEA FILE=WPIX ABB=ON PLU=ON P21/BIX (L) PROTEIN KINAS?/BIX  
L83 951 SEA FILE=WPIX ABB=ON PLU=ON (P21/BIX OR P 21/BIX)  
L84 22202 SEA FILE=WPIX ABB=ON PLU=ON (WRINKL?/BIX OR SKIN WRINKL?/BIX  
OR WRINK? REDUC?/BIX OR SKIN AGING/BIX OR SKIN AGEING/BIX OR  
PHOTO/BIX (L) (AGING/BIX OR AGEING/BIX))  
L85 1 SEA FILE=WPIX ABB=ON PLU=ON (L77 OR L78 OR L79 OR L80) AND  
(L81 OR L82 OR L83) AND L84

=> s 185

L104 1 (L77 OR L78 OR L79 OR L80) AND (L81 OR L82 OR L83) AND L84

=> file biosis

FILE 'BIOSIS' ENTERED AT 16:38:48 ON 28 APR 2006  
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FILE COVERS 1969 TO DATE.  
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT  
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 26 April 2006 (20060426/ED)

=> d que 174

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L65      225 SEA FILE=BIOSIS ABB=ON  PLU=ON  P21 PROTEIN/CT
L66      3066 SEA FILE=BIOSIS ABB=ON  PLU=ON  P21/CT
L67      4 SEA FILE=BIOSIS ABB=ON  PLU=ON  SKIN AGING/CT
L68      2118 SEA FILE=BIOSIS ABB=ON  PLU=ON  (SKIN OR PHOTO) (L) (AGING OR
AGEING)
L69      2403 SEA FILE=BIOSIS ABB=ON  PLU=ON  (WRINKL? OR SKIN WRINKL? OR
WRINK? REDUC?)
L70      1038 SEA FILE=BIOSIS ABB=ON  PLU=ON  ("FUJII S"/AU OR "FUJII S
F"/AU OR "FUJII S I"/AU OR "FUJII S Y KURODA"/AU OR "FUJII
SEISHIRO"/AU)
L71      68 SEA FILE=BIOSIS ABB=ON  PLU=ON  ("DOTTO P"/AU OR "DOTTO P
A"/AU OR "DOTTO P G"/AU OR "DOTTO PAOLA"/AU OR "DOTTO PAOLO"/AU
OR "DOTTO PAOLO D"/AU OR "DOTTO PAOLO G"/AU)
L72      141 SEA FILE=BIOSIS ABB=ON  PLU=ON  ("HAN R"/AU OR "HAN R C"/AU OR
"HAN R F"/AU OR "HAN R I"/AU OR "HAN R J"/AU OR "HAN R J L"/AU
OR "HAN R K"/AU OR "HAN R K W"/AU OR "HAN R M"/AU OR "HAN R
N"/AU OR "HAN R N N"/AU OR "HAN R O"/AU OR "HAN R W"/AU OR
"HAN R Y"/AU OR "HAN R Z"/AU OR "HAN RONG"/AU OR "HAN RONG
LAN"/AU OR "HAN RONG RONG"/AU OR "HAN RONG ZHUANG"/AU)
L73      57 SEA FILE=BIOSIS ABB=ON  PLU=ON  ("BRISSETTE J"/AU OR "BRISSETTE
J C"/AU OR "BRISSETTE J L"/AU OR "BRISSETTE JANICE"/AU OR
"BRISSETTE JANICE L"/AU)
L74      0 SEA FILE=BIOSIS ABB=ON  PLU=ON  (L70 OR L71 OR L72 OR L73) AND
(L65 OR L66) AND (L67 OR L68 OR L69)

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=> s l74

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L105      0 (L70 OR L71 OR L72 OR L73) AND (L65 OR L66) AND (L67 OR L68 OR
L69)

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=> file caplus

FILE 'CAPLUS' ENTERED AT 16:38:50 ON 28 APR 2006  
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FILE COVERS 1907 - 28 Apr 2006 VOL 144 ISS 19  
 FILE LAST UPDATED: 27 Apr 2006 (20060427/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

=> d que l15; d que l61

L1 658 SEA FILE=CAPLUS ABB=ON PLU=ON P21-ACTIVATED KINASE/CT  
 L2 0 SEA FILE=CAPLUS ABB=ON PLU=ON PROTEINS (L) P21/CT  
 L3 0 SEA FILE=CAPLUS ABB=ON PLU=ON PROTEINS (L) SIGNALING+OLD/CT  
 L4 142893 SEA FILE=CAPLUS ABB=ON PLU=ON SIGNAL TRANSDUCTION/CT  
 L5 88152 SEA FILE=CAPLUS ABB=ON PLU=ON (P21 OR P(2A)21 OR P21 PROTEIN  
 KINASE OR P21 SIGNAL TRANSDUCTION? OR P21?)  
 L7 11170 SEA FILE=CAPLUS ABB=ON PLU=ON (WRINKL? OR SKIN WRINKL? OR  
 WRINK? REDUC?)  
 L8 25 SEA FILE=CAPLUS ABB=ON PLU=ON (L1 OR L2 OR L3 OR L4 OR L5)  
 AND L7  
 L11 356 SEA FILE=CAPLUS ABB=ON PLU=ON ("FUJII S"/AU OR "FUJII  
 SEISHIRO"/AU)  
 L12 13 SEA FILE=CAPLUS ABB=ON PLU=ON ("DOTTO P"/AU OR "DOTTO P  
 DEL"/AU OR "DOTTO PAOLA"/AU OR "DOTTO PAOLO"/AU OR "DOTTO  
 PAOLO DEL"/AU)  
 L13 154 SEA FILE=CAPLUS ABB=ON PLU=ON ("HAN R"/AU OR "HAN R D"/AU OR  
 "HAN R F"/AU OR "HAN R J"/AU OR "HAN R K W"/AU OR "HAN R M"/AU  
 OR "HAN R N N"/AU OR "HAN R P"/AU OR "HAN R Q"/AU OR "HAN R  
 S"/AU OR "HAN R T"/AU OR "HAN R X"/AU OR "HAN R Y"/AU OR "HAN  
 RONG"/AU OR "HAN RONG BI"/AU OR "HAN RONG BIN"/AU OR "HAN RONG  
 DI"/AU OR "HAN RONG DIAN"/AU OR "HAN RONG JIANG"/AU OR "HAN  
 RONG RONG"/AU)  
 L14 29 SEA FILE=CAPLUS ABB=ON PLU=ON ("BRISSETTE J"/AU OR "BRISSETTE  
 JANICE"/AU OR "BRISSETTE JANICE L"/AU OR "BRISSETTE JANICE  
 LYNN"/AU)  
 L15 1 SEA FILE=CAPLUS ABB=ON PLU=ON L8 AND (L11 OR L12 OR L13 OR  
 L14)  
  
 L11 356 SEA FILE=CAPLUS ABB=ON PLU=ON ("FUJII S"/AU OR "FUJII  
 SEISHIRO"/AU)  
 L12 13 SEA FILE=CAPLUS ABB=ON PLU=ON ("DOTTO P"/AU OR "DOTTO P  
 DEL"/AU OR "DOTTO PAOLA"/AU OR "DOTTO PAOLO"/AU OR "DOTTO  
 PAOLO DEL"/AU)  
 L13 154 SEA FILE=CAPLUS ABB=ON PLU=ON ("HAN R"/AU OR "HAN R D"/AU OR  
 "HAN R F"/AU OR "HAN R J"/AU OR "HAN R K W"/AU OR "HAN R M"/AU  
 OR "HAN R N N"/AU OR "HAN R P"/AU OR "HAN R Q"/AU OR "HAN R  
 S"/AU OR "HAN R T"/AU OR "HAN R X"/AU OR "HAN R Y"/AU OR "HAN  
 RONG"/AU OR "HAN RONG BI"/AU OR "HAN RONG BIN"/AU OR "HAN RONG  
 DI"/AU OR "HAN RONG DIAN"/AU OR "HAN RONG JIANG"/AU OR "HAN  
 RONG RONG"/AU)  
 L14 29 SEA FILE=CAPLUS ABB=ON PLU=ON ("BRISSETTE J"/AU OR "BRISSETTE  
 JANICE"/AU OR "BRISSETTE JANICE L"/AU OR "BRISSETTE JANICE  
 LYNN"/AU)  
 L56 8 SEA FILE=CAPLUS ABB=ON PLU=ON SKIN, DISEASE (L) AGING+OLD/CT  
 L57 0 SEA FILE=CAPLUS ABB=ON PLU=ON PHOTO AGING/CT  
 L58 5521 SEA FILE=CAPLUS ABB=ON PLU=ON (SKIN OR PHOTO) (L) (AGING OR  
 AGEING)  
 L61 6 SEA FILE=CAPLUS ABB=ON PLU=ON (L56 OR L57 OR L58) AND (L11  
 OR L12 OR L13 OR L14)

=> s l15,l61

L106 6 (L15 OR L61)

=> file embase

FILE 'EMBASE' ENTERED AT 16:38:53 ON 28 APR 2006  
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FILE COVERS 1974 TO 28 Apr 2006 (20060428/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

EMBASE is now updated daily. SDI frequency remains weekly (default)  
and biweekly.

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

=> d que l47

```
L39      106 SEA FILE=EMBASE ABB=ON  PLU=ON  P21 ACTIVATED KINASE?/CT
L40      1517 SEA FILE=EMBASE ABB=ON  PLU=ON  P21 (L) (PROTEIN KINAS? OR
          SIGNAL TRANSDUCT?)
L41      477 SEA FILE=EMBASE ABB=ON  PLU=ON  WRINKLE/CT
L42      2415 SEA FILE=EMBASE ABB=ON  PLU=ON  (WRINKL? OR SKIN WRINKL? OR
          WRINK? REDUC?)
L43      1239 SEA FILE=EMBASE ABB=ON  PLU=ON  ("FUJII S"/AU OR "FUJII S
          I"/AU OR "FUJII S K"/AU OR "FUJII S Y"/AU)
L44      45 SEA FILE=EMBASE ABB=ON  PLU=ON  ("DOTTO P"/AU OR "DOTTO P D
          F"/AU)
L45      206 SEA FILE=EMBASE ABB=ON  PLU=ON  ("HAN R"/AU OR "HAN R C"/AU OR
          "HAN R F"/AU OR "HAN R G"/AU OR "HAN R J"/AU OR "HAN R J L"/AU
          OR "HAN R K"/AU OR "HAN R L"/AU OR "HAN R N"/AU OR "HAN R N
          N"/AU OR "HAN R O"/AU OR "HAN R S"/AU OR "HAN R T"/AU OR "HAN
          R W"/AU OR "HAN R Y"/AU OR "HAN R Y H"/AU OR "HAN R Z"/AU OR
          "HAN RONG QIN"/AU)
L46      25 SEA FILE=EMBASE ABB=ON  PLU=ON  ("BRISSETTE J"/AU OR "BRISSETTE
          J L"/AU)
L47      0 SEA FILE=EMBASE ABB=ON  PLU=ON  (L43 OR L44 OR L45 OR L46) AND
          (L39 OR L40) AND (L41 OR L42)
```

=> s l47

```
L107      0 (L43 OR L44 OR L45 OR L46) AND (L39 OR L40) AND (L41 OR L42)
```

=> file home

FILE 'HOME' ENTERED AT 16:38:55 ON 28 APR 2006

=> => dup rem l103-l107

L103 HAS NO ANSWERS

L105 HAS NO ANSWERS

L107 HAS NO ANSWERS

FILE 'WPIX' ENTERED AT 16:40:56 ON 28 APR 2006

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FILE 'CAPLUS' ENTERED AT 16:40:56 ON 28 APR 2006

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PROCESSING COMPLETED FOR L103

PROCESSING COMPLETED FOR L104

PROCESSING COMPLETED FOR L105

PROCESSING COMPLETED FOR L106

PROCESSING COMPLETED FOR L107

L108 6 DUP REM L103-L107 (1 DUPLICATE REMOVED)  
ANSWER '1' FROM FILE WPIX  
ANSWERS '2-6' FROM FILE CAPLUS

=> d all abs abeq tech 1;d ibib ed abs hitind 2-6

L108 ANSWER 1 OF 6 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN DUPLICATE 1  
AN 2004-295301 [27] WPIX  
DNC C2004-112970  
TI Screening of **wrinkle-reducing** agents useful for  
treating **wrinkles** involves determination of the test agent and  
correlating the ability of the test agent.  
DC B04 D16 D21  
IN BRISSETTE, J; DOTTO, P; FUJII, S; HAN,  
R  
PA (BRIS-I) BRISSETTE J; (DOTT-I) DOTTO P; (FUJI-I) FUJII S; (HANR-I) HAN R;  
(GEHO) GEN HOSPITAL CORP  
CYC 3  
PI WO 2004026249 A2 20040401 (200427)\* EN 20 A61K000-00  
W: CA JP  
US 2004110203 A1 20040610 (200438) C12Q001-00  
JP 2006504932 W 20060209 (200612) 14 G01N033-50  
ADT WO 2004026249 A2 WO 2003-US29496 20030919; US 2004110203 A1 Provisional US  
2002-412503P 20020920, US 2003-664795 20030919; JP 2006504932 W WO  
2003-US29496 20030919, JP 2004-538235 20030919  
FDT JP 2006504932 W Based on WO 2004026249  
PRAI US 2002-412503P 20020920; US 2003-664795 20030919  
IC ICM A61K000-00; C12Q001-00; G01N033-50  
ICS A61K008-00; A61Q017-00; C12Q001-68; G01N033-15  
AB WO2004026249 A UPAB: 20040426  
NOVELTY - Screening of **wrinkles reducing** agent  
involves determination of the test agent to increase or induces a  
component (C1) of the **p21 signal transduction**  
pathway and correlating the ability of the test agent to increase  
expression, activity or levels of (C1) with the agent's ability to reduce  
the appearance or formation of **wrinkles**.  
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:  
(a) a cosmetic composition comprising an agent that increases or  
induces **p21**;  
(b) providing a record involves determination of the test agent to  
increase or induces **p21**;  
(c) generating the record that correlates the ability of the test  
agent; and  
(d) a kit comprises a composition comprising an agent that increases  
or induces (C1); and instructions for using the composition.  
ACTIVITY - Dermatological.  
MECHANISM OF ACTION - None given.  
USE - As a cosmetic for preventing or treating **wrinkles**,  
for reducing the appearance or formation of **wrinkles** on the skin  
(claimed) and in the manufacture of medicament for preventing skin damage  
e.g. UVB-induce skin damage.  
ADVANTAGE - The **p21 signal transduction**  
pathway prevents skin damage, reduces the appearance or formation of  
**wrinkles** on the skin and UVB-induce skin damage.  
Dwg.0/0  
FS CPI  
FA AB  
MC CPI: B04-E02F; B04-E05; B04-F0200E; B04-N0200E; B11-C08E1; B11-C08F2;  
B11-C08F4; B11-C10; B12-K04E; B12-K04F; B14-N17C; B14-R05; D05-H08;

AT 16:51:47 ON 28 APR 2006

D QUE L97

L114 1 SEA ABB=ON PLU=ON L97

FILE 'HOME' ENTERED AT 16:51:52 ON 28 APR 2006

FILE 'STNGUIDE' ENTERED AT 16:52:02 ON 28 APR 2006

FILE 'MEDLINE, WPIX, BIOSIS, CAPLUS, USPATFULL, BIOTECHNO' ENTERED AT  
16:52:54 ON 28 APR 2006

L115 13 DUP REM L109-L114 (0 DUPLICATES REMOVED)

ANSWERS '1-5' FROM FILE MEDLINE

ANSWER '6' FROM FILE WPIX

ANSWERS '7-10' FROM FILE BIOSIS

ANSWER '11' FROM FILE CAPLUS

ANSWER '12' FROM FILE USPATFULL

ANSWER '13' FROM FILE BIOTECHNO

D IALL 1-5

D ALL ABS ABEQ TECH 6

D IALL 7-10

D IBIB ED ABS HITIND 11

D IALL 13

FILE 'USPATFULL' ENTERED AT 17:00:19 ON 28 APR 2006

FILE 'STNGUIDE' ENTERED AT 17:02:08 ON 28 APR 2006

FILE 'USPATFULL' ENTERED AT 17:04:31 ON 28 APR 2006

FILE 'USPATFULL' ENTERED AT 17:04:46 ON 28 APR 2006

D IBIB ABS HIT L100 TOT

=>

OR L22 OR L23) AND (L24 OR L26)

FILE 'WPIX' ENTERED AT 16:38:44 ON 28 APR 2006

D QUE L85

L104 1 SEA ABB=ON PLU=ON (L77 OR L78 OR L79 OR L80) AND (L81 OR L82  
OR L83) AND L84

FILE 'BIOSIS' ENTERED AT 16:38:48 ON 28 APR 2006

D QUE L74

L105 0 SEA ABB=ON PLU=ON (L70 OR L71 OR L72 OR L73) AND (L65 OR  
L66) AND (L67 OR L68 OR L69)

FILE 'CAPLUS' ENTERED AT 16:38:50 ON 28 APR 2006

D QUE L15

D QUE L61

L106 6 SEA ABB=ON PLU=ON (L15 OR L61)

FILE 'EMBASE' ENTERED AT 16:38:53 ON 28 APR 2006

D QUE L47

L107 0 SEA ABB=ON PLU=ON (L43 OR L44 OR L45 OR L46) AND (L39 OR  
L40) AND (L41 OR L42)

FILE 'HOME' ENTERED AT 16:38:55 ON 28 APR 2006

FILE 'STNGUIDE' ENTERED AT 16:39:02 ON 28 APR 2006

FILE 'WPIX, CAPLUS' ENTERED AT 16:40:56 ON 28 APR 2006

L108 6 DUP REM L103-L107 (1 DUPLICATE REMOVED)  
ANSWER '1' FROM FILE WPIX  
ANSWERS '2-6' FROM FILE CAPLUS  
D ALL ABS ABEQ TECH 1  
D IBIB ED ABS HITIND 2-6

FILE 'MEDLINE' ENTERED AT 16:51:32 ON 28 APR 2006

D QUE L55

L109 5 SEA ABB=ON PLU=ON L55 NOT L27

FILE 'WPIX' ENTERED AT 16:51:35 ON 28 APR 2006

D QUE L86

L110 1 SEA ABB=ON PLU=ON L86 NOT L85

FILE 'BIOSIS' ENTERED AT 16:51:38 ON 28 APR 2006

D QUE L76

L111 4 SEA ABB=ON PLU=ON L76 NOT L74

FILE 'CAPLUS' ENTERED AT 16:51:41 ON 28 APR 2006

D QUE L38

D QUE L60

D QUE L88

D QUE L90

D QUE L101

D QUE L102

L112 1 SEA ABB=ON PLU=ON (L38 OR L60 OR L88 OR L90 OR L101 OR L102)  
NOT (L15 OR L61)

FILE 'USPATFULL' ENTERED AT 16:51:44 ON 28 APR 2006

D QUE L100

L113 1 SEA ABB=ON PLU=ON L99 AND L98

FILE 'PASCAL, BIOTECHNO, ESBIODBASE, TOXCENTER, KOSMET, SCISEARCH' ENTERED



```

1  FILE FRFULL
2  FILE GBFULL
4  FILE IFIPAT
2  FILE INPADOC
3  FILE KOSMET
6  FILE MEDLINE
3  FILE NLDB
1  FILE NUTRACEUT
4  FILE PASCAL
1  FILE PATDPAFULL
73 FILE PCTFULL
6  FILE PHIN
7  FILE PROMT
7  FILE SCISEARCH
6  FILE TOXCENTER
178 FILE USPATFULL
26  FILE USPAT2
3   FILE WPIDS
3   FILE WPINDEX
L91  QUE ABB=ON  PLU=ON  (P21 OR P 21) AND (WRINKL? OR PHOTOAG? OR
      SKIN (2A) (AGING OR AGEING))
      -----
      D RANK

      FILE 'PASCAL, BIOTECHNO, ESBIODBASE, TOXCENTER, KOSMET, SCISEARCH' ENTERED
      AT 16:19:35 ON 28 APR 2006
L92  45765 SEA ABB=ON  PLU=ON  (P21 OR P 21)
L93  14267 SEA ABB=ON  PLU=ON  (WRINKL? OR PHOTOAG? OR SKIN (2A) (AGING OR
      AGEING))
L94  30 SEA ABB=ON  PLU=ON  L92 AND L93
L95  11 DUP REM L94 (19 DUPLICATES REMOVED)
      ANSWERS '1-4' FROM FILE PASCAL
      ANSWERS '5-6' FROM FILE BIOTECHNO
      ANSWER '7' FROM FILE ESBIODBASE
      ANSWER '8' FROM FILE TOXCENTER
      ANSWERS '9-11' FROM FILE KOSMET
      D SCAN
L96  1 SEA ABB=ON  PLU=ON  L95 AND DRUG EFFECTS/CT
      D SCAN
L97  1 SEA ABB=ON  PLU=ON  L95 AND DRUG EFFECT/CT
      D SCAN

      FILE 'USPATFULL' ENTERED AT 16:23:38 ON 28 APR 2006
L98  612 SEA ABB=ON  PLU=ON  (P21 OR P 21)/TI,IT,AB,CLM
L99  5951 SEA ABB=ON  PLU=ON  (WRINKL? OR PHOTOAG? OR SKIN (2A) (AGING OR
      AGEING))/TI,IT,AB,CLM
L100 1 SEA ABB=ON  PLU=ON  L99 AND L98
      D SCAN
      D KWIC

      FILE 'CAPLUS' ENTERED AT 16:27:52 ON 28 APR 2006
L101 2 SEA ABB=ON  PLU=ON  L8 AND (P21 OR P 21)
      D SCAN
      D TI L61 1-6
L102 1 SEA ABB=ON  PLU=ON  L61 AND (P21 OR P 21)
      D SCAN

      FILE 'MEDLINE' ENTERED AT 16:38:41 ON 28 APR 2006
      D QUE L27
L103 0 SEA ABB=ON  PLU=ON  (L16 OR L17 OR L18 OR L19) AND (L20 OR L21

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          E SIGNAL TRANSDUCTION/CT
          E PROTEIN/CT
L83      951 SEA ABB=ON  PLU=ON  (P21/BIX OR P 21/BIX)
          E WRINKLES/CT
          E WRINKLE/CT
          E SKIN AGING/CT
L84      22202 SEA ABB=ON  PLU=ON  (WRINKL?/BIX OR SKIN WRINKL?/BIX OR WRINK?
          REDUC?/BIX OR SKIN AGING/BIX OR SKIN AGEING/BIX OR PHOTO/BIX
          (L) (AGING/BIX OR AGEING/BIX))
L85      1 SEA ABB=ON  PLU=ON  (L77 OR L78 OR L79 OR L80) AND (L81 OR L82
          OR L83) AND L84
          D SCAN
L86      2 SEA ABB=ON  PLU=ON  (L81 OR L82 OR L83) AND L84
          D SCAN
          D BROWSE L85

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FILE 'STNGUIDE' ENTERED AT 15:31:34 ON 28 APR 2006

FILE 'WPIX' ENTERED AT 15:44:39 ON 28 APR 2006

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          E A61K000/IPC
          E A61K000-00C
          E A61K000-00/IPC
          E A61K000-00/ICM,ICS,ICA
L*** DEL  464 S E4
          D HIT

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FILE 'STNGUIDE' ENTERED AT 15:46:56 ON 28 APR 2006

FILE 'WPIX' ENTERED AT 15:55:13 ON 28 APR 2006

E AK1K008-00/ICM,ICS,ICA

FILE 'STNGUIDE' ENTERED AT 15:57:44 ON 28 APR 2006

FILE 'WPIX' ENTERED AT 16:00:21 ON 28 APR 2006

FILE 'CAPLUS' ENTERED AT 16:05:03 ON 28 APR 2006

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          D QUE L8
          E SCREENING/CT
          E E4+ALL
          E E2+ALL
L87      46461 SEA ABB=ON  PLU=ON  SCREENING/CW
L88      0 SEA ABB=ON  PLU=ON  L87 AND L8
          D SCAN TI L8
          D QUE L8
L89      734780 SEA ABB=ON  PLU=ON  9/SC,SX
L90      0 SEA ABB=ON  PLU=ON  L8 AND L89

```

INDEX '1MOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE, AGRICOLA, ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE, BABS, BIBLIODATA, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CEABA-VTB, CERAB, ...' ENTERED AT 16:12:22 ON 28 APR 2006

SEA (P21 OR P 21) AND (WRINKL? OR PHOTOAG? OR SKIN (2A) (AGING O

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5   FILE BIOSIS
4   FILE BIOTECHNO
7   FILE CAPLUS
7   FILE EMBASE
25  FILE EPFULL
6   FILE ESBIODBASE

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L64 0 SEA ABB=ON PLU=ON (L62 OR L49) AND (L43 OR L44 OR L45 OR L46)

FILE 'BIOSIS' ENTERED AT 14:09:20 ON 28 APR 2006

E P21/CT

L65 225 SEA ABB=ON PLU=ON P21 PROTEIN/CT

L66 3066 SEA ABB=ON PLU=ON P21/CT

E SKIN AGING/CT

L67 4 SEA ABB=ON PLU=ON SKIN AGING/CT

E PHOTO AGING/CT

L68 2118 SEA ABB=ON PLU=ON (SKIN OR PHOTO) (L) (AGING OR AGEING)

E WRINKLE/CT

L69 2403 SEA ABB=ON PLU=ON (WRINKL? OR SKIN WRINKL? OR WRINK? REDUC?)

FILE 'STNGUIDE' ENTERED AT 14:14:48 ON 28 APR 2006

FILE 'BIOSIS' ENTERED AT 15:00:15 ON 28 APR 2006

E FUJII S/AU

L70 1038 SEA ABB=ON PLU=ON ("FUJII S"/AU OR "FUJII S F"/AU OR "FUJII S I"/AU OR "FUJII S Y KURODA"/AU OR "FUJII SEISHIRO"/AU)

E DOTTO P/AU

L71 68 SEA ABB=ON PLU=ON ("DOTTO P"/AU OR "DOTTO P A"/AU OR "DOTTO P G"/AU OR "DOTTO PAOLA"/AU OR "DOTTO PAOLO"/AU OR "DOTTO PAOLO D"/AU OR "DOTTO PAOLO G"/AU)

E HAN R/AU

L72 141 SEA ABB=ON PLU=ON ("HAN R"/AU OR "HAN R C"/AU OR "HAN R F"/AU OR "HAN R I"/AU OR "HAN R J"/AU OR "HAN R J L"/AU OR "HAN R K"/AU OR "HAN R K W"/AU OR "HAN R M"/AU OR "HAN R N"/AU OR "HAN R N N"/AU OR "HAN R O"/AU OR "HAN R W"/AU OR "HAN R Y"/AU OR "HAN R Z"/AU OR "HAN RONG"/AU OR "HAN RONG LAN"/AU OR "HAN RONG RONG"/AU OR "HAN RONG ZHUANG"/AU)

E BRISSETTE J/AU

L73 57 SEA ABB=ON PLU=ON ("BRISSETTE J"/AU OR "BRISSETTE J C"/AU OR "BRISSETTE J L"/AU OR "BRISSETTE JANICE"/AU OR "BRISSETTE JANICE L"/AU)

L74 0 SEA ABB=ON PLU=ON (L70 OR L71 OR L72 OR L73) AND (L65 OR L66) AND (L67 OR L68 OR L69)

L75 4 SEA ABB=ON PLU=ON (L65 OR L66) AND (L67 OR L68 OR L69)

D SCAN

L76 4 SEA ABB=ON PLU=ON L75 AND (P21 OR P 21)

D KWIC

FILE 'WPIX' ENTERED AT 15:11:11 ON 28 APR 2006

E FUJII S/AU

L77 766 SEA ABB=ON PLU=ON ("FUJII S"/AU OR "FUJII S I C"/AU OR "FUJII S K"/AU OR "FUJII S N"/AU)

E DOTTO P/AU

E DOTTO/AU

L78 3 SEA ABB=ON PLU=ON ("DOTTO G P"/AU OR "DOTTO P"/AU)

E HAN R/AU

L79 118 SEA ABB=ON PLU=ON ("HAN R"/AU OR "HAN R A"/AU OR "HAN R G"/AU OR "HAN R H"/AU OR "HAN R J L"/AU OR "HAN R L"/AU OR "HAN R S"/AU OR "HAN R Y"/AU)

E BRISSETTE J/AU

L80 6 SEA ABB=ON PLU=ON ("BRISSETTE J"/AU OR "BRISSETTE J E"/AU OR "BRISSETTE J W"/AU)

E P21/CT

L81 16 SEA ABB=ON PLU=ON P21/BIX (L) SIGNAL TRANSDUCT?/BIX

L82 39 SEA ABB=ON PLU=ON P21/BIX (L) PROTEIN KINAS?/BIX

L43 1239 SEA ABB=ON PLU=ON ("FUJII S"/AU OR "FUJII S I"/AU OR "FUJII S K"/AU OR "FUJII S Y"/AU)  
E DOTTO P/AU

L44 45 SEA ABB=ON PLU=ON ("DOTTO P"/AU OR "DOTTO P D F"/AU)  
E HAN R/AU

L45 206 SEA ABB=ON PLU=ON ("HAN R"/AU OR "HAN R C"/AU OR "HAN R F"/AU OR "HAN R G"/AU OR "HAN R J"/AU OR "HAN R J L"/AU OR "HAN R K"/AU OR "HAN R L"/AU OR "HAN R N"/AU OR "HAN R N N"/AU OR "HAN R O"/AU OR "HAN R S"/AU OR "HAN R T"/AU OR "HAN R W"/AU OR "HAN R Y"/AU OR "HAN R Y H"/AU OR "HAN R Z"/AU OR "HAN RONG QIN"/AU)  
E BRISSETTE J/AU

L46 25 SEA ABB=ON PLU=ON ("BRISSETTE J"/AU OR "BRISSETTE J L"/AU)

L47 0 SEA ABB=ON PLU=ON (L43 OR L44 OR L45 OR L46) AND (L39 OR L40) AND (L41 OR L42)

L48 0 SEA ABB=ON PLU=ON (L39 OR L40) AND (L41 OR L42)

L49 2464 SEA ABB=ON PLU=ON (SKIN OR PHOTO) (L) (AGING OR AGEING)

L50 0 SEA ABB=ON PLU=ON L49 AND (L39 OR L40)

FILE 'MEDLINE' ENTERED AT 13:58:06 ON 28 APR 2006

E SKIN AGING/CT  
E E3+ALL

L51 2229 SEA ABB=ON PLU=ON SKIN AGING/CT  
E PHOTO AGING/CT

L52 4153 SEA ABB=ON PLU=ON (SKIN OR PHOTO) (L) (AGING OR AGEING)

L53 64 SEA ABB=ON PLU=ON (L51 OR L52) AND (L20 OR L21 OR L22 OR L23)

L54 12 SEA ABB=ON PLU=ON L53 AND (P21 OR P 21)  
D TRIAL  
D KWIC  
D KWIC 2  
D TI 1-12

L55 5 SEA ABB=ON PLU=ON L54 NOT PY>2002  
D KWIC

FILE 'CAPLUS' ENTERED AT 14:01:58 ON 28 APR 2006

E SKIN AGING/CT  
E E3+ALL  
E E2+ALL

L56 8 SEA ABB=ON PLU=ON SKIN, DISEASE (L) AGING+OLD/CT  
E PHOTO AGING/CT

L57 0 SEA ABB=ON PLU=ON PHOTO AGING/CT

L58 5521 SEA ABB=ON PLU=ON (SKIN OR PHOTO) (L) (AGING OR AGEING)

L59 979 SEA ABB=ON PLU=ON (L56 OR L57 OR L58) AND L7

L60 1 SEA ABB=ON PLU=ON L59 AND (P21 OR P 21)  
D SCAN

L61 6 SEA ABB=ON PLU=ON (L56 OR L57 OR L58) AND (L11 OR L12 OR L13 OR L14)  
D KWIC  
D TI 1-6  
D BIB

FILE 'MEDLINE' ENTERED AT 14:05:56 ON 28 APR 2006

FILE 'EMBASE' ENTERED AT 14:07:36 ON 28 APR 2006

E SKIN AGING/CT  
E E3+ALL  
E E2+ALL

L62 669 SEA ABB=ON PLU=ON CUTANEOUS PARAMETERS/CT

L63 0 SEA ABB=ON PLU=ON (L62 OR L49) AND (L39 OR L40)

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E WRINKLE/CT
E E5+ALL
E E2+ALL
L24      2229 SEA ABB=ON  PLU=ON  SKIN AGING/CT
E WRINKLE/CT
E SKIN WRINK/CT
E E4+ALL
E SKIN WRINK/CT
E E5+ALL
E PHOTOAGING/CT
E E4+ALL
L25      0 SEA ABB=ON  PLU=ON  (L16 OR L17 OR L18 OR L19) AND (L20 OR L21
OR L22 OR L23) AND L24
L26      2182 SEA ABB=ON  PLU=ON  (WRINKL? OR SKIN WRINKL? OR WRINK? REDUC?)
L27      0 SEA ABB=ON  PLU=ON  (L16 OR L17 OR L18 OR L19) AND (L20 OR L21
OR L22 OR L23) AND (L24 OR L26)
L28      51 SEA ABB=ON  PLU=ON  (L20 OR L21 OR L22 OR L23) AND (L24 OR
L26)
L29      30 SEA ABB=ON  PLU=ON  L28 NOT PY>2002
L30      0 SEA ABB=ON  PLU=ON  L29 AND (P21 OR P 21)
D TRIAL L29
L31      0 SEA ABB=ON  PLU=ON  L30 AND L23
L32      371 SEA ABB=ON  PLU=ON  P21 (L) SIGNAL TRANSDUCT?
L33      0 SEA ABB=ON  PLU=ON  L32 AND L28
L34      924 SEA ABB=ON  PLU=ON  P21 (L) PROTEIN KINAS?
L35      0 SEA ABB=ON  PLU=ON  L34 AND L28
L36      0 SEA ABB=ON  PLU=ON  (L32 OR L34) AND (L16 OR L17 OR L18 OR
L19)

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FILE 'EMBASE' ENTERED AT 13:43:04 ON 28 APR 2006

FILE 'CAPLUS' ENTERED AT 13:43:15 ON 28 APR 2006

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L37      1259 SEA ABB=ON  PLU=ON  P21 (L) (PROTEIN KINAS? OR SIGNAL TRANSDUCT
?)
L38      1 SEA ABB=ON  PLU=ON  L37 AND L7
D SCAN
D BIB

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FILE 'EMBASE' ENTERED AT 13:45:01 ON 28 APR 2006

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E P21/CT
L39      106 SEA ABB=ON  PLU=ON  P21 ACTIVATED KINASE?/CT
L40      1517 SEA ABB=ON  PLU=ON  P21 (L) (PROTEIN KINAS? OR SIGNAL TRANSDUCT
?)
E SIGNAL TRANSDUCT/CT
E E4+ALL
E SIGNAL TRANSDUCT/CT
E WRINKLE/CT
E E3+ALL
L41      477 SEA ABB=ON  PLU=ON  WRINKLE/CT
E WRINKLE/CT
E E12+ALL
E SKIN AGING/CT
E E3+ALL
E E2+ALL
E SKIN WRINKL/CT
E E4+ALL
L42      2415 SEA ABB=ON  PLU=ON  (WRINKL? OR SKIN WRINKL? OR WRINK? REDUC?)
E FUJII S/AU

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FILE 'CAPLUS' ENTERED AT 13:10:13 ON 28 APR 2006

L10 14 SEA ABB=ON PLU=ON L8 NOT (PY>2002 OR AY>2002 OR PRY>2002)  
 D TI 1-14  
 E PHOTOAGIN/CT  
 E E5+ALL  
 E FUJII S/AU

L11 356 SEA ABB=ON PLU=ON ("FUJII S"/AU OR "FUJII SEISHIRO"/AU)  
 E DOTTO P/AU

L12 13 SEA ABB=ON PLU=ON ("DOTTO P"/AU OR "DOTTO P DEL"/AU OR  
 "DOTTO PAOLA"/AU OR "DOTTO PAOLO"/AU OR "DOTTO PAOLO DEL"/AU)  
 E HAN R/AU

L13 154 SEA ABB=ON PLU=ON ("HAN R"/AU OR "HAN R D"/AU OR "HAN R  
 F"/AU OR "HAN R J"/AU OR "HAN R K W"/AU OR "HAN R M"/AU OR  
 "HAN R N N"/AU OR "HAN R P"/AU OR "HAN R Q"/AU OR "HAN R S"/AU  
 OR "HAN R T"/AU OR "HAN R X"/AU OR "HAN R Y"/AU OR "HAN  
 RONG"/AU OR "HAN RONG BI"/AU OR "HAN RONG BIN"/AU OR "HAN RONG  
 DI"/AU OR "HAN RONG DIAN"/AU OR "HAN RONG JIANG"/AU OR "HAN  
 RONG RONG"/AU)  
 E BRISSETTE J/AU

L14 29 SEA ABB=ON PLU=ON ("BRISSETTE J"/AU OR "BRISSETTE JANICE"/AU  
 OR "BRISSETTE JANICE L"/AU OR "BRISSETTE JANICE LYNN"/AU)

L15 1 SEA ABB=ON PLU=ON L8 AND (L11 OR L12 OR L13 OR L14)  
 D SCAN L10

FILE 'MEDLINE' ENTERED AT 13:25:44 ON 28 APR 2006

E FUJII S/AU

L16 1164 SEA ABB=ON PLU=ON ("FUJII S"/AU OR "FUJII SEISHIRO"/AU)  
 E DOTTO P/AU

L17 26 SEA ABB=ON PLU=ON ("DOTTO P"/AU OR "DOTTO PAOLO"/AU)  
 E HAN R/AU

L18 200 SEA ABB=ON PLU=ON ("HAN R"/AU OR "HAN R C"/AU OR "HAN R  
 F"/AU OR "HAN R J"/AU OR "HAN R K"/AU OR "HAN R L"/AU OR "HAN  
 R N"/AU OR "HAN R O"/AU OR "HAN R S"/AU OR "HAN R X"/AU OR  
 "HAN R Y"/AU OR "HAN R Z"/AU OR "HAN RONG"/AU OR "HAN RONG  
 BIN"/AU)  
 E BRISSETTE J/AU

L19 26 SEA ABB=ON PLU=ON ("BRISSETTE J"/AU OR "BRISSETTE J L"/AU OR  
 "BRISSETTE JANICE L"/AU)  
 E P21/CT  
 E E3+ALL  
 E P21 (RHO) PROTEIN/CT  
 E E3+ALL  
 E E2+ALL

L20 2050 SEA ABB=ON PLU=ON RHO GTP-BINDING PROTEINS/CT  
 E SIGNAL TRANSDUCTION/CT  
 E E3+ALL

L21 171376 SEA ABB=ON PLU=ON SIGNAL TRANSDUCTION+NT/CT  
 E SIGNAL TRANSDUCTION/CT  
 E E5+ALL  
 E SIGNAL TRANSDUCTION/CT  
 E E7+ALL  
 E PROTEINS (L) SIGNALING+OLD/CT  
 E PROTEINS/CT  
 E PROTEINS S/CT  
 E E95+ALL  
 E E2+ALL

L22 1597 SEA ABB=ON PLU=ON INTRACELLULAR SIGNALING PEPTIDES AND  
 PROTEINS/CT

L23 27550 SEA ABB=ON PLU=ON (P21 OR P(2A)21 OR P21 PROTEIN KINASE OR  
 P21 SIGNAL TRANSDUCT?)



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(FILE 'HOME' ENTERED AT 12:45:45 ON 28 APR 2006)

FILE 'CAPLUS' ENTERED AT 12:45:59 ON 28 APR 2006

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      E P21/CT
      E E3+ALL
      E E3+ALL
      E P21/CT
      E E8+ALL
      E P21-ACTIVATED KINASE 1/CT
      E E3+ALL
L1      658 SEA ABB=ON PLU=ON P21-ACTIVATED KINASE/CT
      E P21/CT
      E E3+ALL
L2      0 SEA ABB=ON PLU=ON PROTEINS (L) P21/CT
      E SIGNAL TRANSDUCTION/CT
      E E4+ALL
      E SIGNAL TRANSDUCTION/CT
      E E5+ALL
      E E2+ALL
L3      0 SEA ABB=ON PLU=ON PROTEINS (L) SIGNALING+OLD/CT
      E SIGNAL TRANSDUCTION/CT
      E E6+ALL
      E SIGNAL TRANSDUCTION/CT
      E E9+ALL
L4      142893 SEA ABB=ON PLU=ON SIGNAL TRANSDUCTION/CT
L*** DEL 142893 S SIGNAL TRANSDUCTION, BIOLOGICAL/CT
L*** DEL 0 S L5 NOT L4
L5      88152 SEA ABB=ON PLU=ON (P21 OR P(2A)21 OR P21 PROTEIN KINASE OR
      P21 SIGNAL TRANSDUCTION? OR P21?)
      E WRINKLE/CT
      E WRINKLES/CT
      E E1
      E E3+ALL
      E E2+ALL
L6      0 SEA ABB=ON PLU=ON COSMETICS (L) CREAMS, WRINKLE-PREVENTING/CT
      E WRINKLES/CT
      E E2+ALL
      E E2+ALL
      E SKIN AGIN/CT
      E E4+ALL
      E E2+ALL
      E SKIN WRINKL/CT
L7      11170 SEA ABB=ON PLU=ON (WRINKL? OR SKIN WRINKL? OR WRINK? REDUC?)
L8      25 SEA ABB=ON PLU=ON (L1 OR L2 OR L3 OR L4 OR L5) AND L7

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FILE 'STNGUIDE' ENTERED AT 13:01:54 ON 28 APR 2006

FILE 'CAPLUS' ENTERED AT 13:03:52 ON 28 APR 2006

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L9      2 SEA ABB=ON PLU=ON L8 AND (P(2A)21)
      D SCAN
      D KWIC
      D KWIC 2

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FILE 'STNGUIDE' ENTERED AT 13:05:43 ON 28 APR 2006



20. A method of providing a record, the method comprising: providing a test agent; determining whether the test agent increases or induces **p21**; and generating a record that correlates the ability of the test agent to increase expression, activity or levels of **p21** with the agent's ability to reduce the appearance or formation of **wrinkles**, thereby providing a record.

21. A method of providing **wrinkle** protection to a subject, said method comprising: supplying to the subject a composition that increases or induces a component of the a **p21** signal transduction pathway; and supplying to the subject instructions for using said composition to prevent or reduce **wrinkles**.

22. The method of claim 20, wherein the component of the a **p21** signal transduction pathway is **p21**.

25. A kit for preventing **wrinkles** in a subject, said kit comprising: a composition comprising an agent that increases or induces a component of the **p21** signal transduction pathway; and instructions for using the composition to prevent **wrinkles**.

26. The kit of claim 25, wherein said component of the a **p21** signal transduction pathway is **p21**.

IT     **Skin, disease**  
          (**aging, wrinkles**; methods and compns. for  
          preventing skin damage)  
IT     **Proteins**  
          (**p21**; methods and compns. for preventing skin damage)

=>

and/or reduce UVB-induced skin damage, e.g., **wrinkles**. The method includes identifying an agent that increases or induces the expression, activity or levels of a component of the **p21** signal transduction pathway. Also included are methods and compositions for treating UVB-induced skin damage.

CLM

What is claimed is:

1. A method of screening for an agent that reduces the appearance or formation of **wrinkles**, the method comprising: providing a test agent; determining whether the test agent increases or induces a component of the **p21** signal transduction pathway; and correlating the ability of a test agent to increase expression, activity or levels of a component of the **p21** signal transduction pathway with the agent's ability to reduce the appearance or formation of **wrinkles**, thereby screening for an agent that reduces the appearance or formation of **wrinkles**.

2. The method of claim 1, further comprising evaluating the effect of the agent on **wrinkles** on the skin of a subject.

3. The method of claim 1, further comprising selecting a test agent that increases expression, activity or levels of a component of the **p21** signal transduction.

4. The method of claim 1, wherein the determining step comprises determining if the test agent increases or induces **p21**.

6. The method of claim 1, wherein the determining step comprises: (a) providing a cell, tissue or non-human subject comprising an exogenous nucleic acid comprising a regulatory region of a component of the **p21** signal transduction pathway operably linked to a nucleotide sequence encoding a reporter polypeptide; and (b) evaluating the ability of the test agent to increase the activity of the reporter polypeptide in the cell, tissue or non-human subject, wherein the test agent is determined to increase or induce a component of the **p21** signal transduction pathway if it increases the activity of the reporter polypeptide.

7. The method of claim 4, wherein the determining step comprises: (a) providing a cell, tissue or non-human subject comprising an exogenous nucleic acid comprising a **p21** regulatory region operably linked to a nucleotide sequence encoding a reporter polypeptide; and (b) evaluating the ability of the test agent to increase the activity of the reporter polypeptide in the cell, tissue or non-human subject, wherein the test agent is determined to increase or induce **p21** if it increases the activity of the reporter polypeptide.

11. The method of claim 2, wherein the effect of the agent on UVB-induced **wrinkles** is evaluated.

12. A method of preventing or treating **wrinkles**, the method comprising: (a) identifying a subject in need of prevention or treatment of **wrinkles**; and (b) administering to the subject an agent that increases or induces a component of the **p21** signal transduction pathway.

14. The method of claim 12, wherein the component of the **p21** signal transduction pathway is **p21**.

16. A cosmetic composition comprising an agent that increases or induces **p21**.

IT Interferons  
 RL: BIOL (Biological study)  
 (α2-, gene for, of human, conformational **wrinkle** in regulatory region of)

IT 9002-64-6 9002-72-6 66796-54-1  
 RL: PRP (Properties)  
 (gene for, of cattle and human, conformational **wrinkle** in regulatory region of)

IT 9004-10-8, biological studies  
 RL: BIOL (Biological study)  
 (gene for, of dog, conformational **wrinkle** in regulatory region of)

IT 9000-90-2  
 RL: PRP (Properties)  
 (gene for, of mouse, conformational **wrinkle** in regulatory region of)

IT 74749-30-7  
 RL: PRP (Properties)  
 (gene for, of rat, conformational **wrinkle** in regulatory region of)

=> d ibib abs hit 1100 tot

L100 ANSWER 1 OF 1 USPATFULL on STN

ACCESSION NUMBER: 2004:144539 USPATFULL  
 TITLE: Methods and compositions for preventing skin damage  
 INVENTOR(S): Fujii, Seishiro, Boston, MA, UNITED STATES  
 Dotto, Paolo, Boston, MA, UNITED STATES  
 Han, Rong, Boston, MA, UNITED STATES  
 Brissette, Janice, Charlestown, MA, UNITED STATES

|                     | NUMBER         | KIND | DATE          |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 2004110203  | A1   | 20040610      |
| APPLICATION INFO.:  | US 2003-664795 | A1   | 20030919 (10) |

|                       | NUMBER   | DATE          |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 2002-412503P  | 20020920 (60) |
| DOCUMENT TYPE:        | Utility  |               |
| FILE SEGMENT:         | APPLICATION  |               |
| LEGAL REPRESENTATIVE: | FISH & RICHARDSON PC, 225 FRANKLIN ST, BOSTON, MA, 02110 |               |
| NUMBER OF CLAIMS:     | 28   |               |
| EXEMPLARY CLAIM:      | 1  |               |
| LINE COUNT:           | 649  |               |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention features methods of screening for compounds that prevent and/or reduce UVB-induced skin damage, e.g., **wrinkles**. The method includes identifying an agent that increases or induces the expression, activity or levels of a component of the **p21** signal transduction pathway. Also included are methods and compositions for treating UVB-induced skin damage.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention features methods of screening for compounds that prevent

- RL: PRP (Properties)  
(gene for, of rat, conformational **wrinkle** in regulatory region of)
- IT Ribonucleic acids, ribosomal  
RL: BIOL (Biological study)  
(gene for, of *Xenopus laevis*, conformational **wrinkle** in regulatory region of)
- IT Eukaryote  
(genes of, conformational **wrinkle** in regulatory region of)
- IT Gene and Genetic element, animal  
RL: BIOL (Biological study)  
(of eukaryotes, conformational **wrinkle** in regulatory region of)
- IT Conformation and Conformers  
(of **wrinkle**, in eukaryote gene regulatory region)
- IT Histones  
RL: BIOL (Biological study)  
(H1, gene for, of sea urchin, conformational **wrinkle** in regulatory region of)
- IT Histones  
RL: BIOL (Biological study)  
(H4, gene for, of sea urchin, conformational **wrinkle** in regulatory region of)
- IT Metallothioneins  
RL: BIOL (Biological study)  
(II, gene for, of human, conformation **wrinkle** in regulatory region of)
- IT Virus, animal  
(Moloney murine leukemia, genes of, conformational **wrinkle** in regulatory region of)
- IT Proteins  
RL: BIOL (Biological study)  
(P21, gene for, of Harvey murine sarcoma virus, conformational **wrinkle** in regulatory region of)
- IT Ribonucleic acids  
RL: BIOL (Biological study)  
(U1, gene for, of human, conformation **wrinkle** in regulatory region of)
- IT Virus, animal  
(adeno-, genes of, conformational **wrinkle** in regulatory region of)
- IT Ribonucleic acids, transfer  
RL: BIOL (Biological study)  
(aspartic acid-specific, gene for, of rat, conformational **wrinkle** in regulatory region of)
- IT Ribonucleic acids, transfer  
RL: BIOL (Biological study)  
(glycine-specific, gene for, of rat, conformational **wrinkle** in regulatory region of)
- IT Virus, animal  
(herpes simplex, genes of, conformational **wrinkle** in regulatory region of)
- IT Proteins  
RL: BIOL (Biological study)  
(steroid-binding, gene for, of rat prostate, conformational **wrinkle** in regulatory region of)
- IT Gene and Genetic element, animal  
RL: BIOL (Biological study)  
(Y, of chicken, conformational **wrinkle** in regulatory region of)

osteoporosis: bone disease  
Osteoporosis (MeSH)

INDEX TERMS: Diseases  
skin atrophy: integumentary system disease

INDEX TERMS: Chemicals & Biochemicals  
Brcal: full-length isoform; p21; p53

INDEX TERMS: Miscellaneous Descriptors  
aging; body fat deposition; malignant transformation;  
senescence; tumorigenesis

ORGANISM: Classifier  
Muridae 86375  
Super Taxa  
Rodentia; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
mouse (common): adult  
Taxa Notes  
Animals, Chordates, Mammals, Nonhuman Vertebrates,  
Nonhuman Mammals, Rodents, Vertebrates

L115 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1985:608001 CAPLUS

DOCUMENT NUMBER: 103:208001

TITLE: Structural wrinkles and the genomic  
regulatory sites of eukaryotes

AUTHOR(S): Nussinov, Ruth

CORPORATE SOURCE: Lab. Mol. Genet., Natl. Inst. Child Health Hum. Dev.,  
Bethesda, MD, 20205, USA

SOURCE: Journal of Molecular Evolution (1985), 22(2), 150-9  
CODEN: JMEVAU; ISSN: 0022-2844

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 28 Dec 1985

AB Calcns. of DNA angular parameters in 50 eukaryotic sequences reveal  
regions of large conformational deviations from ideal DNA around  
regulatory sites. Frequently, discrete peaks of structural variation are  
present upstream of genes. Known regulatory regions often include  
variants of consensus sequences. Thus, imprecise sequences and structures  
are recognized within large genomic stretches. The existence of  
structurally wrinkled regions in the vicinity of regulatory  
sequences is likely to facilitate greatly their recognition by proteins  
and enzymes.

CC 3-3 (Biochemical Genetics)  
Section cross-reference(s): 6, 10, 12, 13

IT Immunoglobulins

RL: BIOL (Biological study)  
(gene for  $\kappa$  chain of, of mouse, conformational wrinkle  
in regulatory region of)

IT Keratins

Ovalbumins

RL: BIOL (Biological study)  
(gene for, of chicken, conformational wrinkle in regulatory  
region of)

IT Globulins

RL: BIOL (Biological study)  
(gene for, of eukaryote, conformation wrinkle in regulatory  
region of)

IT Actins

REGISTRY NUMBER: 9001-12-1 (matrix metalloproteinase-1)  
60-40-2 (mecamylamine)  
54-11-5 (nicotine)  
260524-81-0 (GenBank-AB040450)  
279212-93-0 (GenBank-AB043585)  
136218-12-7 (GenBank-M37981)  
384427-81-0 (GenBank-M64349)  
140831-43-2 (GenBank-M83712)  
384591-99-5 (GenBank-U13737)  
171752-05-9 (GenBank-U40583)  
174387-61-2 (GenBank-U48861)  
391554-91-9 (GenBank-U62437)

L115 ANSWER 10 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN

ACCESSION NUMBER: 2003:88211 BIOSIS  
DOCUMENT NUMBER: PREV200300088211  
TITLE: Senescence, aging, and malignant transformation mediated by  
p53 in mice lacking the Brcal full-length isoform.  
AUTHOR(S): Cao, Liu; Li, Wenmei; Kim, Sangsoo; Brodie, Steven G.;  
Deng, Chu-Xia [Reprint Author]  
CORPORATE SOURCE: Genetics of Development and Diseases Branch, National  
Institutes of Diabetes and Digestive and Kidney Diseases,  
National Institutes of Health, Bethesda, MD, 20892, USA  
chuxiad@bdg10.niddk.nih.gov  
SOURCE: Genes & Development, (January 15 2003) Vol. 17, No. 2, pp.  
201-213. print.  
CODEN: GEDEEP. ISSN: 0890-9369.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 12 Feb 2003  
Last Updated on STN: 12 Feb 2003

ABSTRACT: Senescence may function as a two-edged sword that brings unexpected  
consequences to organisms. Here we provide evidence to support this theory by  
showing that the absence of the Brcal full-length isoform causes senescence in  
mutant embryos and cultured cells as well as **aging** and tumorigenesis  
in adult mice. Haploid loss of p53 overcame embryonic senescence but failed to  
prevent the adult mutant mice from prematurely **aging**, which included  
decreased life span, reduced body fat deposition, osteoporosis, **skin**  
atrophy, and decreased wound healing. We further demonstrate that mutant cells  
that escaped senescence had undergone clonal selection for faster proliferation  
and extensive genetic/molecular alterations, including overexpression of cyclin  
D1 and cyclin A and loss of p53. These observations provide the first in vivo  
evidence that links cell senescence to **aging** due to impaired function  
of Brcal at the expense of tumorigenesis.

CONCEPT CODE: Biochemistry studies - General 10060  
Biochemistry studies - Proteins, peptides and amino acids  
10064  
Bones, joints, fasciae, connective and adipose tissue -  
Pathology 18006  
Integumentary system - Pathology 18506  
Neoplasms - Pathology, clinical aspects and systemic  
effects 24004  
Gerontology 24500  
INDEX TERMS: Major Concepts  
Aging; Biochemistry and Molecular Biophysics; Tumor  
Biology  
INDEX TERMS: Diseases  
decreased wound healing: integumentary system disease  
INDEX TERMS: Diseases

functioning, leading to changes in **skin** homeostasis. Using RT-PCR and Western blotting, we found that a 24-hour exposure of human DF to 10  $\mu$ M Nic causes a 1.9- to 28-fold increase of the mRNA and protein levels of the cell cycle regulators p21, cyclin D1, Ki-67, and PCNA and a 1.7- to 2-fold increase of the apoptosis regulators Bcl-2 and caspase 3. Nic exposure also up-regulated expression of the dermal matrix proteins collagen type I  $\alpha$ 1 and elastin as well as matrix metalloproteinase-1. Mecamylamine (Mec), the specific antagonist of nAChRs, abolished Nic-induced alterations, indicating that they resulted from a pharmacologic stimulation of nAChRs expressed by DF. To establish the relevance of these findings to a specific nicotinic pathway, we studied human DF transfected with anti- $\alpha$ 3 antisense oligonucleotides and murine DF from  $\alpha$ 3 nAChR knockout mice. In both cases, lack of  $\alpha$ 3 was associated with alterations in fibroblast growth and function that were opposite to those observed in DF treated with Nic, suggesting that the nicotinic effects on DF were mostly mediated by  $\alpha$ 3 nAChR. In addition to  $\alpha$ 3, the nAChR subunits detected in human DF were  $\alpha$ 5,  $\alpha$ 7,  $\beta$ 2, and  $\beta$ 4. The exposure of DF to Nic altered the relative amounts of each of these subunits, leading to reciprocal changes in (3H)epibatidine-binding kinetics. Thus, some of the pathobiologic effects of tobacco products on extracellular matrix turnover in the **skin** may stem from Nic-induced alterations in the physiologic control of the unfolding of the genetically determined program of growth and the tissue remodeling function of DF as well as alterations in the structure and function of fibroblast nAChRs.

CONCEPT CODE: Cytology - Animal 02506  
 Biochemistry studies - General 10060  
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062  
 Biochemistry studies - Proteins, peptides and amino acids 10064  
 Integumentary system - Physiology and biochemistry 18504  
 Toxicology - General and methods 22501

INDEX TERMS: Major Concepts  
 Toxicology

INDEX TERMS: Parts, Structures, & Systems of Organisms  
 dermal fibroblast; integumentary system; skin;  
 integumentary system

INDEX TERMS: Chemicals & Biochemicals  
 Ki-67; PCNA; [tritiated hydrogen]epibatidine;  $\alpha$ -3  
 nicotinic acetylcholine receptor; anti- $\alpha$ -3 antisense  
 oligonucleotides; collagen type I; cyclin D1; elastin;  
 matrix metalloproteinase-1; mecamylamine; nicotine;  
 toxicity; nicotinic acetylcholine receptors; p21

INDEX TERMS: Sequence Data  
 AB040450: GenBank, nucleotide sequence; AB043585:  
 GenBank, nucleotide sequence; JO4038: nucleotide  
 sequence; M37981: GenBank, nucleotide sequence; M64349:  
 GenBank, nucleotide sequence; M83712: GenBank,  
 nucleotide sequence; NM-000088: nucleotide sequence;  
 NM-000501: nucleotide sequence; NM-002421: nucleotide  
 sequence; NM-138578: nucleotide sequence; U13737:  
 GenBank, nucleotide sequence; U40583: GenBank,  
 nucleotide sequence; U48861: GenBank, nucleotide  
 sequence; U62437: GenBank, nucleotide sequence

INDEX TERMS: Methods & Equipment  
 RT-PCR: genetic techniques, laboratory techniques;  
 Western blotting: genetic techniques, laboratory  
 techniques

INDEX TERMS: Miscellaneous Descriptors  
 tobacco products

Integumentary system - Physiology and biochemistry 18504  
Integumentary system - Pathology 18506

INDEX TERMS: Major Concepts  
Integumentary System (Chemical Coordination and Homeostasis)

INDEX TERMS: Parts, Structures, & Systems of Organisms  
epidermal cell: integumentary system

INDEX TERMS: Diseases  
seborrheic keratosis: integumentary system disease, pathology  
Keratosis, Seborrheic (MeSH)

INDEX TERMS: Chemicals & Biochemicals  
DNA; cyclin A: expression; cyclin D: expression; cyclin E: expression; p16: expression; **p21: expression**; p53: expression; retinoblastoma protein: expression; telomerase-associated protein 1 [TP1]

INDEX TERMS: Miscellaneous Descriptors  
DNA fragmentation; G-1 arrest; survival time

ORGANISM: Classifier  
Hominidae 86215  
Super Taxa  
Primates; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
human (common)  
Taxa Notes  
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L115 ANSWER 9 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
ACCESSION NUMBER: 2003:141899 BIOSIS  
DOCUMENT NUMBER: PREV200300141899  
TITLE: Central role of fibroblast alpha3 nicotinic acetylcholine receptor in mediating cutaneous effects of nicotine.

AUTHOR(S): Arredondo, Juan; Hall, Leon L.; Ndoye, Assane; Nguyen, Vu Thuong; Chernyavsky, Alexander I.; Bercovich, Dani; Orr-Urtreger, Avi; Beaudet, Arthur L.; Grando, Sergei A. [Reprint Author]

CORPORATE SOURCE: Department of Dermatology, University of California Davis Medical Center, 4860 Y Street, Suite 3400, Sacramento, CA, 95817, USA  
sagrando@ucdavis.edu

SOURCE: Laboratory Investigation, (February 2003) Vol. 83, No. 2, pp. 207-225. print.  
CODEN: LAINAW. ISSN: 0023-6837.

DOCUMENT TYPE: Article  
LANGUAGE: English

OTHER SOURCE: GenBank-AB040450; GenBank-AB043585; GenBank-M37981; GenBank-M64349; GenBank-M83712; GenBank-U13737; GenBank-U40583; GenBank-U48861; GenBank-U62437

ENTRY DATE: Entered STN: 19 Mar 2003  
Last Updated on STN: 9 May 2003

ABSTRACT: Smoking is associated with aberrant cutaneous tissue remodeling, such as precocious **skin aging** and impaired wound healing. The mechanism is not fully understood. Dermal fibroblasts (DF) are the primary cellular component of the dermis and may provide a target for pathobiologic effects of tobacco products. The purpose of this study was to characterize a mechanism of nicotine (Nic) effects on the growth and tissue remodeling function of DF. We hypothesized that the effects of Nic on DF result from its binding to specific nicotinic acetylcholine receptors (nAChRs) expressed by these cells and that downstream signaling from the receptors alters normal cell



## Taxa Notes

Animals, Chordates, Humans, Mammals, Primates,  
Vertebrates

REGISTRY NUMBER: 9031-11-2 (beta-galactosidase)  
9031-11-2 (EC 3.2.1.23)  
7440-47-3 (chromium)

L115 ANSWER 8 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:547465 BIOSIS

DOCUMENT NUMBER: PREV200300549209

TITLE: Enhanced expression of p 6 in seborrhoeic keratosis; a  
lesion of accumulated senescent epidermal cells in G1  
arrest.

AUTHOR(S): Nakamura, S. [Reprint Author]; Nishioka, K.

CORPORATE SOURCE: Department of Environmental Immunodermatology, Tokyo  
Medical and Dental University, Graduate School, Yushima  
1-5-45, Bunkyo-ku, Tokyo, 113-8519, Japan  
ruggle@mbk.sphere.ne.jp

SOURCE: British Journal of Dermatology, (September 2003) Vol. 149,  
No. 3, pp. 560-565. print.  
CODEN: BJDEAZ. ISSN: 0007-0963.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 19 Nov 2003

Last Updated on STN: 19 Nov 2003

ABSTRACT:Background Seborrhoeic keratosis (SK) is a common skin  
disease associated with skin ageing and photoageing, but  
only limited studies have been performed on SK and the senescence of  
keratinocytes. Objectives We sought to clarify the genetic basis of SK and the  
senescence of keratinocytes. Methods Expression of p16, cyclins A, D and E,  
\*\*\*p21\*\*\*, p53, retinoblastoma (Rb) gene product and telomerase-associated  
protein 1 (TP1) in SK was examined by immunohistochemistry. DNA fragmentation  
in SK was detected by the terminal deoxynucleotidyl transferase-mediated  
deoxyuridine triphosphate-biotin nick end labelling method. We cultured  
keratinocytes from SK lesions and non-lesional epidermis and examined  
expression of p16, observed morphology of the cultured cells by light and  
electron microscopy and measured survival time. Results p16, a  
cyclin-dependent kinase inhibitor, was expressed in all cells from SK lesions,  
whereas normal keratinocytes expressed p16 only in the granular cells. Other  
factors such as cyclins A, D and E, p21, p53, Rb gene product, and  
TP1, were not expressed in SK cells. These results suggest that p16  
expression is a marker of SK and that p16 has a role in the pathogenesis of SK.  
DNA fragmentation was not detected in four of five SK tissue samples; one of  
the SK tissue samples showed DNA fragmentation only in the superficial upper  
layer of an SK lesion, suggesting that apoptosis was inhibited in SK cells. In  
contrast, normal epidermis showed DNA fragmentation in the granular and  
squamous layers. Immunohistochemical examination of cultured SK cells also  
revealed the presence of p16. A greater number of SK cells survived after 3  
weeks of culture in comparison with normal keratinocytes. Features of  
senescence, such as a balloon-like appearance after lengthy culture and  
increased amounts of tonofilaments in cytoplasm, were observed in SK cells in  
culture. Conclusions These results suggest that SK is a benign neoplasm where  
keratinocytes in a senescent condition and G1 arrest are accumulated.

CONCEPT CODE: Cytology - Animal 02506

Cytology - Human 02508

Biochemistry studies - Nucleic acids, purines and  
pyrimidines 10062

Biochemistry studies - Proteins, peptides and amino acids  
10064

Pathology - General 12502

1079-1087. print.  
ISSN: 0531-5565 (ISSN print).

DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 24 Nov 2004  
Last Updated on STN: 24 Nov 2004

ABSTRACT: Heavy metals like CrVI, CdII, PbII and Still have many applications in industry. They also represent a group of labour pollutants, as they are involved in several physiological disorders, such as carcinogenesis and various tissue dysfunctions. However, limited knowledge exists regarding their effects on **ageing**. In the current work we provide evidence that workers chronically exposed to CrVI have considerably reduced serum levels of the biomarker of senescence and cell survival, Apolipoprotein J/Clusterin (ApoJ/CLU). Moreover, we have found that both the degree and the time of exposure to CrVI associate negatively with ApoJ/CLU serum levels. To further examine whether CrVI directly affects cellular senescence we treated for 10 weeks two adult **skin** fibroblasts cultures as well as embryonic fibroblasts with a range of CrVI concentrations that approximate the values recorded in the blood circulation of exposed workers. Cellular treatment with a CrVI concentration that approximates the highest concentration in the blood was extremely toxic and nearly all cells died immediately after the first treatment. Interestingly, continuous treatment with a 10-fold lower CrVI concentration resulted in the induction of premature senescence. More specifically, treated cells were growth arrested, acquired an irregular shape, were positive to P-galactosidase staining, accumulated oxidized proteins and over-expressed the cyclin-dependent kinase inhibitor **p21** and ApoJ/CLU. Similar treatments with three additional labour pollutants resulted in the induction of premature senescence by CdII, but not by Still or PbII. In summary, our results indicate that exposure to CrVI induces alterations of senescence biomarkers both in vivo and in vitro. They also provide new valuable tools for monitoring CrVI cytotoxic effects in vivo as well as for re-evaluating the maximum permissive values of some labour pollutants, like CrVI and CdII. Copyright 2004 Elsevier Inc. All rights reserved.

CONCEPT CODE: Biochemistry studies - General 10060  
Biochemistry studies - Minerals 10069  
Enzymes - General and comparative studies: coenzymes 10802  
Blood - Blood and lymph studies 15002  
Blood - Blood cell studies 15004  
Gerontology 24500  
Public health - Occupational health 37013

INDEX TERMS: Major Concepts  
Aging; Biochemistry and Molecular Biophysics;  
Occupational Health (Allied Medical Sciences)

INDEX TERMS: Parts, Structures, & Systems of Organisms  
serum: blood and lymphatics

INDEX TERMS: Chemicals & Biochemicals  
apolipoprotein J; beta-galactosidase [EC 3.2.1.23];  
biomarkers; chromium; clusterin; cyclin-dependent kinase  
inhibitor; heavy metal; labour pollutants; **p21**

INDEX TERMS: Methods & Equipment  
staining: laboratory techniques

INDEX TERMS: Miscellaneous Descriptors  
aging; cell survival; cellular senescence

ORGANISM: Classifier  
Hominidae 86215  
Super Taxa  
Primates; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
human (common): adult, male

of environmental toxins including solar radiation comprising applying (C);  
(3) treating skin inflammatory conditions arising from stimuli such as exposure to allergies, solar radiation or skin infection comprising applying to cells (C);

(4) increasing cell mass comprises applying to cells (C); and

(5) a pharmaceutical composition comprising (C) in combination with a pharmaceutically acceptable carrier.

ACTIVITY - Antiinflammatory; antiageing.

Acetyl-carnosine was shown to markedly delay the onset of senescence of cells by increasing the lifespan of MRC-5 cells in culture. This was confirmed by rejuvenation experiments. The morphology of cells grown in media supplemented with acetyl-carnosine was distinct from the controls. In control flasks cells were broad and flat with long processes extending to other cells. In fact some cells began to extend bipolar processes. Cells became very granular and debris accumulated in the medium. This morphology was typical of senescent cells. However, cells grown in media supplemented with acetyl-carnosine were long and spindle and gave an appearance of steaming. Cell growth showed confluency and cells acquired a phenotype typical of younger cells. To confirm this rejuvenation of senescent cells by acetyl-carnosine the expression of 3 known biomarkers used were p21, p27 and p16 and are all cyclin-dependent kinase inhibitors and are expressed at different stages of the cell cycle. In both cases non-senescent cultures show about a 30% of nuclei unstained while essentially all nuclei stain in senescent cultures. Once cells started to exhibit some degree of nuclei staining indicating senescence, old media was replaced with media supplemented with acetyl-carnosine, and after a few days, cells began to adopt a younger phenotype and there was no expression of p16 in the nucleus.

MECHANISM OF ACTION - None given.

USE - The novel method is used for altering the senescence of cells, and in the preparation of medicament for treating aging, degenerative-related diseases, slowing down aging of skin and skin inflammatory conditions (claimed).

ADVANTAGE - N-acetyl carnosine has superior anti-ageing properties than prior use of L-carnosine. Longevity growth curves showed that N-acetyl carnosine allowed more population doublings (PDs) than controls and significantly more PDs than carnosine itself. In addition, N-acetyl carnosine was found to be almost completely resistant to attack by human blood peptidases.

Dwg.0/0

TECH UPTX: 20020618

TECHNOLOGY FOCUS - BIOLOGY - Preferred Cells: The cells are human fibroblast cells, such as human fetal lung fibroblasts.

L115 ANSWER 7 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STM  
ACCESSION NUMBER: 2004:453400 BIOSIS  
DOCUMENT NUMBER: PREV200400452193  
TITLE: Alterations of senescence biomarkers in human cells by exposure to CrVI in vivo and in vitro.  
AUTHOR(S): Katsiki, Magda; Trougakos, Ioannis P.; Chondrogianni, Niki; Alexopoulos, Evangelos C.; Makropoulos, Vassilis; Gonos, Efsthios S. [Reprint Author]  
CORPORATE SOURCE: Lab Mol and Cellular Ageing Inst Biol Res and Biotechnol, Natl Hellen Res Fdn, 48 Vas Constantinou Ave, Athens, 11635, Greece  
sgonos@eie.gr  
SOURCE: Experimental Gerontology, (July 2004) Vol. 39, No. 7, pp.

which characterize **skin aging** including skin texture, changes in pigmentation or discoloration, diminution of immunoreactiveness, increased sensitivity to toxic and genotoxic effects of environmental toxins including solar radiation comprising applying (C);

(3) treating skin inflammatory conditions arising from stimuli such as exposure to allergies, solar radiation or skin infection comprising applying to cells (C);

(4) increasing cell mass comprises applying to cells (C); and

(5) a pharmaceutical composition comprising (C) in combination with a pharmaceutically acceptable carrier.

ACTIVITY - Antiinflammatory; antiageing.

Acetyl-carnosine was shown to markedly delay the onset of senescence of cells by increasing the lifespan of MRC-5 cells in culture. This was confirmed by rejuvenation experiments. The morphology of cells grown in media supplemented with acetyl-carnosine was distinct from the controls. In control flasks cells were broad and flat with long processes extending to other cells. In fact some cells began to extend bipolar processes. Cells became very granular and debris accumulated in the medium. This morphology was typical of senescent cells. However, cells grown in media supplemented with acetyl-carnosine were long and spindle and gave an appearance of streaming. Cell growth showed confluency and cells acquired a phenotype typical of younger cells. To confirm this rejuvenation of senescent cells by acetyl-carnosine the expression of 3 known biomarkers used were p21, p27 and p16 and are all cyclin-dependent kinase inhibitors and are expressed at different stages of the cell cycle. In both cases non-senescent cultures show about a 30% of nuclei unstained while essentially all nuclei stain in senescent cultures. Once cells started to exhibit some degree of nuclei staining indicating senescence, old media was replaced with media supplemented with acetyl-carnosine, and after a few days, cells began to adopt a younger phenotype and there was no expression of p16 in the nucleus.

MECHANISM OF ACTION - None given.

USE - The novel method is used for altering the senescence of cells, and in the preparation of medicament for treating aging, degenerative-related diseases, slowing down aging of skin and skin inflammatory conditions (claimed).

ADVANTAGE - N-acetyl carnosine has superior anti-ageing properties than prior use of L-carnosine. Longevity growth curves showed that N-acetyl carnosine allowed more population doublings (PDs) than controls and significantly more PDs than carnosine itself. In addition, N-acetyl carnosine was found to be almost completely resistant to attack by human blood peptidases.

Dwg.0/0

FS CPI  
FA AB; DCN  
MC CPI: B07-D09; B14-C03; B14-N17  
AN 2002-352125 [38] WPIX  
AB WO 200226940 A UPAB: 20020618

NOVELTY - Altering the senescence of cells, or a combination of delaying the onset, preventing or reversing the senescence of cells, comprising applying to cells a composition (C) that includes N-acetyl-carnosine as an active ingredient, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) treating aging or degenerative related diseases in a subject, comprises applying to cells (C);

(2) slowing down aging of skin and the development of those features which characterize **skin aging** including skin texture, changes in pigmentation or discoloration, diminution of immunoreactiveness, increased sensitivity to toxic and genotoxic effects

in human fibroblasts. However, their inactivation may enhance the probability of spontaneous immortalization.

CONTROLLED TERM: \*Cell Aging: PH, physiology  
**Cyclin-Dependent Kinase Inhibitor p21**  
 \*Cyclins: ME, metabolism  
 Fibroblasts: ME, metabolism  
 \*Fibroblasts: PH, physiology  
 Humans  
 Li-Fraumeni Syndrome: ME, metabolism  
 \*Li-Fraumeni Syndrome: PA, pathology  
 Research Support, U.S. Gov't, P.H.S.  
 Tumor Suppressor Protein p53: ME, metabolism  
 CHEMICAL NAME: 0 (CDKN1A protein, human); 0 (Cyclin-Dependent Kinase Inhibitor p21); 0 (Cyclins); 0 (Tumor Suppressor Protein p53)

L115 ANSWER 6 OF 13 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN  
 AN 2002-352125 [38] WPIX  
 DNC C2002-100114  
 TI Altering the senescence of cells for treating aging, degenerative-related diseases or skin allergies, comprises application of a composition of N-acetyl-Carnosine.  
 DC B04  
 IN GRIGG, G W; MALLOY, P; MOLLOY, P  
 PA (BETA-N) BETA PEPTIDE FOUND PTY LTD; (CSIR) COMMONWEALTH SCI & IND RES ORG; (GRIG-I) GRIGG G W; (MOLL-I) MOLLOY P  
 CYC 97  
 PI WO 2002026940 A1 20020404 (200238)\* EN 23 C12N005-06  
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
 NL OA PT SD SE SL SZ TR TZ UG ZW  
 W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CO CR CU CZ DE DK DM  
 DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ  
 LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PH PL PT RO RU SD  
 SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW  
 AU 2001093484 A 20020408 (200252) C12N005-06  
 EP 1328620 A1 20030723 (200350) EN C12N005-06  
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
 RO SE SI TR  
 US 2004014814 A1 20040122 (200407) A61K031-198  
 ADT WO 2002026940 A1 WO 2001-AU1199 20010925; AU 2001093484 A AU 2001-93484 20010925; EP 1328620 A1 EP 2001-973818 20010925, WO 2001-AU1199 20010925; US 2004014814 A1 WO 2001-AU1199 20010925, US 2003-381057 20030728  
 FDT AU 2001093484 A Based on WO 2002026940; EP 1328620 A1 Based on WO 2002026940  
 PRAI AU 2000-382 20000926  
 IC ICM A61K031-198; C12N005-06  
 ICS A61K031-4172; A61P017-00; C12N005-08  
 AB WO 200226940 A UPAB: 20020618  
 NOVELTY - Altering the senescence of cells, or a combination of delaying the onset, preventing or reversing the senescence of cells, comprising applying to cells a composition (C) that includes N-acetyl-carnosine as an active ingredient, is new.  
 DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:  
 (1) treating aging or degenerative related diseases in a subject, comprises applying to cells (C);  
 (2) slowing down aging of skin and the development of those features

CONTROLLED TERM: Actins: GE, genetics  
\*Actins: ME, metabolism  
Adult  
\*Aging: ME, metabolism  
Cells, Cultured  
Cyclin-Dependent Kinase Inhibitor p21  
Cyclins: GE, genetics  
\*Cyclins: ME, metabolism  
Epidermis: CY, cytology  
Epidermis: EM, embryology  
Epidermis: ME, metabolism  
Fetus: ME, metabolism  
Fibroblasts: CY, cytology  
Fibroblasts: ME, metabolism  
Humans  
Procollagen: GE, genetics  
\*Procollagen: ME, metabolism  
RNA, Messenger: ME, metabolism  
Research Support, Non-U.S. Gov't  
Research Support, U.S. Gov't, P.H.S.  
CHEMICAL NAME: 0 (Actins); 0 (CDKN1A protein, human); 0 (Cyclin-Dependent Kinase Inhibitor p21); 0 (Cyclins); 0 (Procollagen); 0 (RNA, Messenger)

L115 ANSWER 5 OF 13 MEDLINE on STN  
ACCESSION NUMBER: 96438605 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 8840965  
TITLE: Expression of p21 is not required for senescence of human fibroblasts.  
AUTHOR: Medcalf A S; Klein-Szanto A J; Cristofalo V J  
CORPORATE SOURCE: Center for Gerontological Research, Medical College of Pennsylvania and Hahnemann University, Philadelphia 19129, USA.  
CONTRACT NUMBER: AG00131 (NIA)  
AG00378 (NIA)  
AG00532 (NIA)  
+  
SOURCE: Cancer research, (1996 Oct 15) Vol. 56, No. 20, pp. 4582-5.  
Journal code: 2984705R. ISSN: 0008-5472.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199611  
ENTRY DATE: Entered STN: 19 Dec 1996  
Last Updated on STN: 19 Dec 1996  
Entered Medline: 4 Nov 1996

ABSTRACT:  
Senescence and immortalization have been studied in skin fibroblasts derived from two individuals with the Li-Fraumeni syndrome. These cells inherit one wild-type and one mutant p53 allele and lose the former during culture. Despite this loss, cultures of Li-Fraumeni syndrome cells progressed normally from early passage to replicative senescence. Senescent cells also expressed barely detectable levels of p21 mRNA, and, in marked contrast to normal cultured cells, levels of p21 expression decreased during in vitro aging. Further maintenance for up to 10 months of post-mitotic cultures has led to the isolation of cells with an extended lifespan. Four potentially immortal cultures have continued to proliferate, and two have completed more than 110 population doublings. These results indicate that p53 and p21 are not required for replicative senescence

Transcription Factors: ME, metabolism  
Transcription, Genetic  
\*Tretinoin: PD, pharmacology  
Ultraviolet Rays  
Up-Regulation  
p38 Mitogen-Activated Protein Kinases  
CAS REGISTRY NO.: 302-79-4 (Tretinoin)  
CHEMICAL NAME: 0 (ATF2 protein, human); 0 (Activating Transcription Factor 2); 0 (Antineoplastic Agents); 0 (Cyclic AMP Response Element-Binding Protein); 0 (Nerve Tissue Proteins); 0 (Proto-Oncogene Proteins c-jun); 0 (Transcription Factor AP-1); 0 (Transcription Factors); EC 2.7.1.112 (Receptor, Epidermal Growth Factor); EC 2.7.1.123 (Ca(2+)-Calmodulin Dependent Protein Kinase); EC 2.7.1.37 (JNK Mitogen-Activated Protein Kinases); EC 2.7.1.37 (Mitogen-Activated Protein Kinases); EC 2.7.1.37 (p38 Mitogen-Activated Protein Kinases); EC 3.6.5.2 (HRAS protein, human); EC 3.6.5.2 (Proto-Oncogene Proteins p21(ras))

L115 ANSWER 4 OF 13 MEDLINE on STN  
ACCESSION NUMBER: 97370256 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 9226632  
TITLE: Abundance of alpha 1(I) and alpha 1(III) procollagen and p21 mRNAs in fibroblasts cultured from fetal and postnatal dermis.  
AUTHOR: Furth J J; Allen R G; Tresini M; Keogh B; Cristofalo V J  
CORPORATE SOURCE: Center for Gerontological Research, Allegheny University of The Health Sciences, Philadelphia, PA 19129-1191, USA.  
CONTRACT NUMBER: AG 00378 (NIA)  
AG 00523 (NIA)  
AG00131 (NIA)  
SOURCE: Mechanisms of ageing and development, (1997 Aug) Vol. 97, No. 2, pp. 131-42.  
Journal code: 0347227. ISSN: 0047-6374.  
PUB. COUNTRY: Ireland  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199709  
ENTRY DATE: Entered STN: 22 Sep 1997  
Last Updated on STN: 22 Sep 1997  
Entered Medline: 11 Sep 1997

ABSTRACT:  
The steady-state abundance of alpha 1(I) and alpha 1(III) procollagen mRNAs, p21Sd11 mRNA, and beta-actin mRNA was determined in 29 skin fibroblast lines established from fetal, young and old donors. Donor ages ranged from 12 gestational weeks to nonagenarian. Adult donors were members of the Baltimore Longitudinal Study of Aging. The abundance of alpha 1(I) procollagen mRNA was decreased in cell lines from both young and old donors compared with fetal lines. Additionally, one alpha 1(I) transcript observed in the fetal lines was not detected in postnatal lines. The abundance of alpha 1(III) procollagen mRNA was decreased in postnatal lines from old donors compared with fetal lines. The abundance of beta-actin mRNA was lower in postnatal lines from both young and old donors compared to fetal lines. These results suggest that cultures of fetal skin fibroblasts exhibit a greater capacity for synthesis of procollagens and beta-actin than postnatal lines. In contrast, the abundance of p21Sd11 mRNA was elevated in lines established from postnatal donors. These results are consistent with developmental changes in amounts of procollagen, beta-actin and p21.

Entered Medline: 23 Apr 1998

## ABSTRACT:

Human **skin** is exposed daily to solar ultraviolet (UV) radiation. UV induces the matrix metalloproteinases collagenase, 92-kD gelatinase, and stromelysin, which degrade **skin** connective tissue and may contribute to premature **skin aging** (photoaging). Pretreatment of **\*\*\*skin\*\*\*** with all-trans retinoic acid (tRA) inhibits UV induction of matrix metalloproteinases. We investigated upstream signal transduction pathways and the mechanism of tRA inhibition of UV induction of matrix metalloproteinases in human **skin** in vivo. Exposure of human **skin** in vivo to low doses of UV activated EGF receptors, the GTP-binding regulatory protein p21Ras, and stimulated mitogen-activated protein (MAP) kinases, extracellular signal-regulated kinase (ERK), c-Jun amino-terminal kinase (JNK), and p38. Both JNK and p38 phosphorylated, and thereby activated transcription factors c-Jun and activating transcription factor 2 (ATF-2), which bound to the c-Jun promoter and upregulated c-Jun gene expression. Elevated c-Jun, in association with constitutively expressed c-Fos, formed increased levels of transcription factor activator protein (AP) 1, which is required for transcription of matrix metalloproteinases. Pretreatment of human **skin** with tRA inhibited UV induction of c-Jun protein and, consequently, AP-1. c-Jun protein inhibition occurred via a posttranscriptional mechanism, since tRA did not inhibit UV induction of c-Jun mRNA. These data demonstrate, for the first time, activation of MAP kinase pathways in humans in vivo, and reveal a novel posttranscriptional mechanism by which tRA antagonizes UV activation of AP-1 by inhibiting c-Jun protein induction. Inhibition of c-Jun induction likely contributes to the previously reported prevention by tRA of UV induction of AP-1-regulated matrix-degrading metalloproteinases in human **skin**.

CONTROLLED TERM:     Activating Transcription Factor 2  
                           \*Antineoplastic Agents: PD, pharmacology  
                           Ca(2+)-Calmodulin Dependent Protein Kinase: ME, metabolism  
                           Ca(2+)-Calmodulin Dependent Protein Kinase: PD, pharmacology  
                           Ca(2+)-Calmodulin Dependent Protein Kinase: RE, radiation effects  
                           Cyclic AMP Response Element-Binding Protein: ME, metabolism  
                           Gene Expression  
                           Humans  
                           JNK Mitogen-Activated Protein Kinases  
                           Mitogen-Activated Protein Kinases: ME, metabolism  
                           Mitogen-Activated Protein Kinases: PD, pharmacology  
                           Mitogen-Activated Protein Kinases: RE, radiation effects  
                           Nerve Tissue Proteins: ME, metabolism  
                           Nerve Tissue Proteins: PD, pharmacology  
                           Nerve Tissue Proteins: RE, radiation effects  
                           Promoter Regions (Genetics)  
                           \*Proto-Oncogene Proteins c-jun: GE, genetics  
                           \*Proto-Oncogene Proteins c-jun: ME, metabolism  
                               Proto-Oncogene Proteins p21(ras): ME, metabolism  
                               Proto-Oncogene Proteins p21(ras): PD, pharmacology  
                               Proto-Oncogene Proteins p21(ras): RE, radiation effects  
                           Receptor, Epidermal Growth Factor: ME, metabolism  
                           Receptor, Epidermal Growth Factor: RE, radiation effects  
                           Research Support, Non-U.S. Gov't  
                           Signal Transduction: GE, genetics  
                           \*Skin: DE, drug effects  
                           Skin: ME, metabolism  
                           \*Skin: RE, radiation effects  
                           Transcription Factor AP-1: ME, metabolism



the irradiated keratinocytes was 75% at 24 h post-irradiation. Various cytokeratins and transcription factors were up-regulated within 1 h post-irradiation. After 6 h, expression of a variety of genes related to growth regulation (e.g. p21(WAF1), notch 4, and smoothened), apoptosis (e.g. caspase 10, hTRIP, and CRAF1), DNA repair (ERCC1, XRCC1), cytokines (e.g. IL-6, IL-13, TGF-beta, and endothelin 2), and cell adhesion (e.g. RhoE, and RhoGDI) were altered in human keratinocytes. These data suggest the changes in a cascade of gene expression in human keratinocytes occurring within 24 h after UVB exposure. Although the roles of these cellular genes after UVB-irradiation remain to be elucidated, microarray analysis may provide a new view of gene expression in epidermal keratinocytes following UVB exposure.

CONTROLLED TERM: Apoptosis  
Cell Survival: RE, radiation effects  
Cell Transformation, Neoplastic  
Cytokines: GE, genetics  
DNA Repair  
DNA, Complementary  
Dose-Response Relationship, Radiation  
Endothelins: GE, genetics  
\*Gene Expression Regulation: RE, radiation effects  
Growth Substances: GE, genetics  
Humans  
Keratin: GE, genetics  
Keratinocytes: CY, cytology  
Keratinocytes: PH, physiology  
\*Keratinocytes: RE, radiation effects  
Oligonucleotide Array Sequence Analysis  
RNA, Messenger: GE, genetics  
Research Support, Non-U.S. Gov't  
Transcription Factors: GE, genetics  
Transcription, Genetic: RE, radiation effects  
\*Ultraviolet Rays

CAS REGISTRY NO.: 68238-35-7 (Keratin)  
CHEMICAL NAME: 0 (Cytokines); 0 (DNA, Complementary); 0 (Endothelins); 0 (Growth Substances); 0 (RNA, Messenger); 0 (Transcription Factors)

L115 ANSWER 3 OF 13 MEDLINE on STN  
ACCESSION NUMBER: 1998171532 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 9502786  
TITLE: Retinoic acid inhibits induction of c-Jun protein by ultraviolet radiation that occurs subsequent to activation of mitogen-activated protein kinase pathways in human skin in vivo.  
AUTHOR: Fisher G J; Talwar H S; Lin J; Lin P; McPhillips F; Wang Z; Li X; Wan Y; Kang S; Voorhees J J  
CORPORATE SOURCE: Department of Dermatology, University of Michigan Medical School, Ann Arbor, Michigan 48109-0609, USA.. dianemch@umich.edu  
SOURCE: The Journal of clinical investigation, (1998 Mar 15) Vol. 101, No. 6, pp. 1432-40. Journal code: 7802877. ISSN: 0021-9738.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 199804  
ENTRY DATE: Entered STN: 30 Apr 1998  
Last Updated on STN: 15 Oct 2002

genotoxic insults into growth arrest and apoptotic signaling pathways that ultimately determine cell fate. As a result of its complex interactions with cell cycle machinery and response to mutagenic agents, p21(WAF1) also has stage-specific roles in epithelial carcinogenesis. Finally, a view is emerging of p21(WAF1) as not merely a cyclin-dependent kinase inhibitor, but also as a direct participant in regulating genes involved in growth arrest, senescence, and **aging**, thus providing an additional layer of control over matters of the cell cycle. This review discusses these various roles played by p21(WAF1) in cell cycle control, and attempts to relate these to epithelial cell biology, with special emphasis on keratinocytes.

CONTROLLED TERM: Apoptosis: PH, physiology  
Cell Cycle: PH, physiology  
Cell Division: PH, physiology  
Cyclin-Dependent Kinase Inhibitor p21  
\*Cyclin-Dependent Kinases: AI, antagonists & inhibitors  
Cyclins: GE, genetics  
\*Cyclins: PH, physiology  
\*Enzyme Inhibitors: PD, pharmacology  
Epithelial Cells: PH, physiology  
Gene Expression Regulation  
Humans  
Keratinocytes: PH, physiology  
Mouth Mucosa: CY, cytology  
Mutagens: PD, pharmacology  
Neoplasms: PA, pathology  
Skin: CY, cytology

CHEMICAL NAME: 0 (CDKN1A protein, human); 0 (Cyclin-Dependent Kinase Inhibitor p21); 0 (Cyclins); 0 (Enzyme Inhibitors); 0 (Mutagens); EC 2.7.1.37 (Cyclin-Dependent Kinases)

L115 ANSWER 2 OF 13 MEDLINE on STN

ACCESSION NUMBER: 2001490518 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11532376

TITLE: Expression profiling of cancer-related genes in human keratinocytes following non-lethal ultraviolet B irradiation.

AUTHOR: Murakami T; Fujimoto M; Ohtsuki M; Nakagawa H

CORPORATE SOURCE: Department of Dermatology, Jichi Medical School, 3311-1 Yakushi-ji, Minamikawachi-machi, Kawachi-gun, Tochigi 329-0498, Japan.. takmu@jichi.ac.jp

SOURCE: Journal of dermatological science, (2001 Oct) Vol. 27, No. 2, pp. 121-9.  
Journal code: 9011485. ISSN: 0923-1811.

PUB. COUNTRY: Ireland

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200110

ENTRY DATE: Entered STN: 5 Sep 2001  
Last Updated on STN: 29 Oct 2001  
Entered Medline: 25 Oct 2001

## ABSTRACT:

Ultraviolet B irradiation initiates and promotes **skin** cancers, **\*\*\*photo\*\*\* -aging**, and immune suppression. In order to elucidate the effect of these processes at the level of gene expression, we used cDNA microarray technology to examine the effect of ultraviolet B irradiation on 588 cancer-related genes in human keratinocytes at 1, 6, and 24 h post-irradiation with a mildly cytotoxic dose of ultraviolet B (170 mJ/cm(2)). The viability of

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PROCESSING COMPLETED FOR L110  
PROCESSING COMPLETED FOR L111  
PROCESSING COMPLETED FOR L112  
PROCESSING COMPLETED FOR L113  
PROCESSING COMPLETED FOR L114  
PROCESSING COMPLETED FOR L114  
PROCESSING COMPLETED FOR L114  
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PROCESSING COMPLETED FOR L114

L115 13 DUP REM L109-L114 (0 DUPLICATES REMOVED)

ANSWERS '1-5' FROM FILE MEDLINE

ANSWER '6' FROM FILE WPIX

ANSWERS '7-10' FROM FILE BIOSIS

ANSWER '11' FROM FILE CAPLUS

ANSWER '12' FROM FILE USPATFULL

ANSWER '13' FROM FILE BIOTECHNO

=> d iall 1-5;d all abs abeq tech 6;d iall 7-10;d ibib ed abs hitind 11; d ibib ed  
abs hitind 12;d iall 13

L115 ANSWER 1 OF 13 MEDLINE on STN  
ACCESSION NUMBER: 2002736836 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12499239  
TITLE: P21Waf1 control of epithelial cell cycle and cell fate.  
AUTHOR: Weinberg Wendy C; Denning Mitchell F  
CORPORATE SOURCE: Laboratory of Immunobiology, Division of Monoclonal  
Antibodies, Center for Biologics Evaluation and Research,  
FDA, NIH Bldg 29B, Room 3NN04, HFM-564, Bethesda, MD 20892,  
USA.. weinberg@cber.fda.gov  
SOURCE: Critical reviews in oral biology and medicine : an official  
publication of the American Association of Oral Biologists,  
(2002) Vol. 13, No. 6, pp. 453-64. Ref: 143  
Journal code: 9009999. ISSN: 1045-4411.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
LANGUAGE: English  
FILE SEGMENT: Dental Journals; Priority Journals  
ENTRY MONTH: 200303  
ENTRY DATE: Entered STN: 27 Dec 2002  
Last Updated on STN: 31 Mar 2003  
Entered Medline: 28 Mar 2003

ABSTRACT:

As a broad-acting cyclin-dependent kinase inhibitor, p21(WAF1)  
occupies a central position in the cell cycle regulation of self-renewing  
tissues such as oral mucosa and skin. In addition to regulating  
normal cell cycle progression decisions, p21(WAF1) integrates

=> file pascal biotechno esbiobase toxcenter kosmet scisearch

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=> d que 197

L92 45765 SEA (P21 OR P 21)

L93 14267 SEA (WRINKL? OR PHOTOAG? OR SKIN (2A) (AGING OR AGEING))

L94 30 SEA L92 AND L93

L95 11 DUP REM L94 (19 DUPLICATES REMOVED)

L97 1 SEA L95 AND DRUG EFFECT/CT

=> s 197

'CT' IS NOT A VALID FIELD CODE

'CT' IS NOT A VALID FIELD CODE

L114 1 L97

=> file home

FILE 'HOME' ENTERED AT 16:51:52 ON 28 APR 2006

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L\*\*\* HAS NO ANSWERS

L\*\*\* HAS NO ANSWERS

L\*\*\* HAS NO ANSWERS

L\*\*\* HAS NO ANSWERS

L\*\*\* HAS NO ANSWERS

DUPLICATE IS NOT AVAILABLE IN 'KOSMET'.

ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE

'1' ANSWERS REMOVED DUE TO ANSWER OVERLAP

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FILE 'WPIX' ENTERED AT 16:52:54 ON 28 APR 2006

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AND L7  
 L101 2 SEA FILE=CAPLUS ABB=ON PLU=ON L8 AND (P21 OR P 21)

L11 356 SEA FILE=CAPLUS ABB=ON PLU=ON ("FUJII S"/AU OR "FUJII SEISHIRO"/AU)  
 L12 13 SEA FILE=CAPLUS ABB=ON PLU=ON ("DOTTO P"/AU OR "DOTTO P DEL"/AU OR "DOTTO PAOLA"/AU OR "DOTTO PAOLO"/AU OR "DOTTO PAOLO DEL"/AU)  
 L13 154 SEA FILE=CAPLUS ABB=ON PLU=ON ("HAN R"/AU OR "HAN R D"/AU OR "HAN R F"/AU OR "HAN R J"/AU OR "HAN R K W"/AU OR "HAN R M"/AU OR "HAN R N N"/AU OR "HAN R P"/AU OR "HAN R Q"/AU OR "HAN R S"/AU OR "HAN R T"/AU OR "HAN R X"/AU OR "HAN R Y"/AU OR "HAN RONG"/AU OR "HAN RONG BI"/AU OR "HAN RONG BIN"/AU OR "HAN RONG DI"/AU OR "HAN RONG DIAN"/AU OR "HAN RONG JIANG"/AU OR "HAN RONG RONG"/AU)  
 L14 29 SEA FILE=CAPLUS ABB=ON PLU=ON ("BRISSETTE J"/AU OR "BRISSETTE JANICE"/AU OR "BRISSETTE JANICE L"/AU OR "BRISSETTE JANICE LYNN"/AU)  
 L56 8 SEA FILE=CAPLUS ABB=ON PLU=ON SKIN, DISEASE (L) AGING+OLD/CT  
 L57 0 SEA FILE=CAPLUS ABB=ON PLU=ON PHOTO AGING/CT  
 L58 5521 SEA FILE=CAPLUS ABB=ON PLU=ON (SKIN OR PHOTO) (L) (AGING OR AGEING)  
 L61 6 SEA FILE=CAPLUS ABB=ON PLU=ON (L56 OR L57 OR L58) AND (L11 OR L12 OR L13 OR L14)  
 L102 1 SEA FILE=CAPLUS ABB=ON PLU=ON L61 AND (P21 OR P 21)

=> s 138,160,188,190,1101,1102 not 115,161

L112 1 (L38 OR L60 OR L88 OR L90 OR L101 OR L102) NOT (L15 OR L61)

=> file uspatfull

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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 27 Apr 2006 (20060427/PD)  
 FILE LAST UPDATED: 27 Apr 2006 (20060427/ED)  
 HIGHEST GRANTED PATENT NUMBER: US7036150  
 HIGHEST APPLICATION PUBLICATION NUMBER: US2006090232  
 CA INDEXING IS CURRENT THROUGH 27 Apr 2006 (20060427/UPCA)  
 ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 27 Apr 2006 (20060427/PD)  
 REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2006  
 USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2006

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L98 612 SEA FILE=USPATFULL ABB=ON PLU=ON (P21 OR P 21)/TI,IT,AB,CLM  
 L99 5951 SEA FILE=USPATFULL ABB=ON PLU=ON (WRINKL? OR PHOTOAG? OR SKIN (2A) (AGING OR AGEING))/TI,IT,AB,CLM  
 L100 1 SEA FILE=USPATFULL ABB=ON PLU=ON L99 AND L98

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L113 1 L99 AND L98

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| L7  | 11170  | SEA FILE=CAPLUS ABB=ON | PLU=ON | (WRINKL? OR SKIN WRINKL? OR WRINK? REDUC?)                                 |
| L37 | 1259   | SEA FILE=CAPLUS ABB=ON | PLU=ON | P21 (L) (PROTEIN KINAS? OR SIGNAL TRANSDUCT?)                              |
| L38 | 1      | SEA FILE=CAPLUS ABB=ON | PLU=ON | L37 AND L7   |
|     |        |                        |        |  |
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| L58 | 5521   | SEA FILE=CAPLUS ABB=ON | PLU=ON | (SKIN OR PHOTO) (L) (AGING OR AGEING)                                      |
| L59 | 979    | SEA FILE=CAPLUS ABB=ON | PLU=ON | (L56 OR L57 OR L58) AND L7   |
| L60 | 1      | SEA FILE=CAPLUS ABB=ON | PLU=ON | L59 AND (P21 OR P 21)  |
|     |        |                        |        |  |
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| L2  | 0      | SEA FILE=CAPLUS ABB=ON | PLU=ON | PROTEINS (L) P21/CT  |
| L3  | 0      | SEA FILE=CAPLUS ABB=ON | PLU=ON | PROTEINS (L) SIGNALING+OLD/CT  |
| L4  | 142893 | SEA FILE=CAPLUS ABB=ON | PLU=ON | SIGNAL TRANSDUCTION/CT   |
| L5  | 88152  | SEA FILE=CAPLUS ABB=ON | PLU=ON | (P21 OR P(2A)21 OR P21 PROTEIN KINASE OR P21 SIGNAL TRANSDUCTION? OR P21?) |
| L7  | 11170  | SEA FILE=CAPLUS ABB=ON | PLU=ON | (WRINKL? OR SKIN WRINKL? OR WRINK? REDUC?)                                 |
| L8  | 25     | SEA FILE=CAPLUS ABB=ON | PLU=ON | (L1 OR L2 OR L3 OR L4 OR L5) AND L7  |
| L87 | 46461  | SEA FILE=CAPLUS ABB=ON | PLU=ON | SCREENING/CW   |
| L88 | 0      | SEA FILE=CAPLUS ABB=ON | PLU=ON | L87 AND L8   |
|     |        |                        |        |  |
| L1  | 658    | SEA FILE=CAPLUS ABB=ON | PLU=ON | P21-ACTIVATED KINASE/CT  |
| L2  | 0      | SEA FILE=CAPLUS ABB=ON | PLU=ON | PROTEINS (L) P21/CT  |
| L3  | 0      | SEA FILE=CAPLUS ABB=ON | PLU=ON | PROTEINS (L) SIGNALING+OLD/CT  |
| L4  | 142893 | SEA FILE=CAPLUS ABB=ON | PLU=ON | SIGNAL TRANSDUCTION/CT   |
| L5  | 88152  | SEA FILE=CAPLUS ABB=ON | PLU=ON | (P21 OR P(2A)21 OR P21 PROTEIN KINASE OR P21 SIGNAL TRANSDUCTION? OR P21?) |
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| L8  | 25     | SEA FILE=CAPLUS ABB=ON | PLU=ON | (L1 OR L2 OR L3 OR L4 OR L5) AND L7  |
| L89 | 734780 | SEA FILE=CAPLUS ABB=ON | PLU=ON | 9/SC, SX   |
| L90 | 0      | SEA FILE=CAPLUS ABB=ON | PLU=ON | L8 AND L89   |
|     |        |                        |        |  |
| L1  | 658    | SEA FILE=CAPLUS ABB=ON | PLU=ON | P21-ACTIVATED KINASE/CT  |
| L2  | 0      | SEA FILE=CAPLUS ABB=ON | PLU=ON | PROTEINS (L) P21/CT  |
| L3  | 0      | SEA FILE=CAPLUS ABB=ON | PLU=ON | PROTEINS (L) SIGNALING+OLD/CT  |
| L4  | 142893 | SEA FILE=CAPLUS ABB=ON | PLU=ON | SIGNAL TRANSDUCTION/CT   |
| L5  | 88152  | SEA FILE=CAPLUS ABB=ON | PLU=ON | (P21 OR P(2A)21 OR P21 PROTEIN KINASE OR P21 SIGNAL TRANSDUCTION? OR P21?) |
| L7  | 11170  | SEA FILE=CAPLUS ABB=ON | PLU=ON | (WRINKL? OR SKIN WRINKL? OR WRINK? REDUC?)                                 |
| L8  | 25     | SEA FILE=CAPLUS ABB=ON | PLU=ON | (L1 OR L2 OR L3 OR L4 OR L5)   |

L110 1 L86 NOT L85

=> file biosis

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FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 26 April 2006 (20060426/ED)

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| L65 | 225  | SEA FILE=BIOSIS | ABB=ON | PLU=ON | P21 PROTEIN/CT                             |
| L66 | 3066 | SEA FILE=BIOSIS | ABB=ON | PLU=ON | P21/CT                                     |
| L67 | 4    | SEA FILE=BIOSIS | ABB=ON | PLU=ON | SKIN AGING/CT                              |
| L68 | 2118 | SEA FILE=BIOSIS | ABB=ON | PLU=ON | (SKIN OR PHOTO) (L) (AGING OR AGEING)      |
| L69 | 2403 | SEA FILE=BIOSIS | ABB=ON | PLU=ON | (WRINKL? OR SKIN WRINKL? OR WRINK? REDUC?) |
| L75 | 4    | SEA FILE=BIOSIS | ABB=ON | PLU=ON | (L65 OR L66) AND (L67 OR L68 OR L69)       |
| L76 | 4    | SEA FILE=BIOSIS | ABB=ON | PLU=ON | L75 AND (P21 OR P 21)                      |

=> s 176 not 174

L111 4 L76 NOT L74

=> file caplus

FILE 'CAPLUS' ENTERED AT 16:51:41 ON 28 APR 2006  
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FILE COVERS 1907 - 28 Apr 2006 VOL 144 ISS 19  
FILE LAST UPDATED: 27 Apr 2006 (20060427/ED)

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<http://www.cas.org/infopolicy.html>

=> d que 138;d que 160; d que 188; d que 190; d que 1101; d que 1102

=> d que 155

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L20      2050 SEA FILE=MEDLINE ABB=ON  PLU=ON  RHO GTP-BINDING PROTEINS/CT
L21      171376 SEA FILE=MEDLINE ABB=ON  PLU=ON  SIGNAL TRANSDUCTION+NT/CT
L22      1597 SEA FILE=MEDLINE ABB=ON  PLU=ON  INTRACELLULAR SIGNALING
          PEPTIDES AND PROTEINS/CT
L23      27550 SEA FILE=MEDLINE ABB=ON  PLU=ON  (P21 OR P(2A)21 OR P21
          PROTEIN KINASE OR P21 SIGNAL TRANSDUCT?)
L51      2229 SEA FILE=MEDLINE ABB=ON  PLU=ON  SKIN AGING/CT
L52      4153 SEA FILE=MEDLINE ABB=ON  PLU=ON  (SKIN OR PHOTO) (L) (AGING OR
          AGEING)
L53      64 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L51 OR L52) AND (L20 OR L21
          OR L22 OR L23)
L54      12 SEA FILE=MEDLINE ABB=ON  PLU=ON  L53 AND (P21 OR P 21)
L55      5 SEA FILE=MEDLINE ABB=ON  PLU=ON  L54 NOT PY>2002

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=> s 155 not 127

L109 5 L55 NOT L27

=> file wpix

FILE 'WPIX' ENTERED AT 16:51:35 ON 28 APR 2006  
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FILE LAST UPDATED: 26 APR 2006 <20060426/UP>  
 MOST RECENT DERWENT UPDATE: 200627 <200627/DW>  
 DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,  
 PLEASE VISIT:  
[http://www.stn-international.de/training\\_center/patents/stn\\_guide.pdf](http://www.stn-international.de/training_center/patents/stn_guide.pdf) <

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE  
<http://scientific.thomson.com/support/patents/coverage/latestupdates/>

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE  
[http://www.stn-international.de/stndatabases/details/ipc\\_reform.html](http://www.stn-international.de/stndatabases/details/ipc_reform.html) and  
<http://scientific.thomson.com/media/scpdf/ipcrdwpf.pdf> <<<

>>> UPCOMING NEW DWPI: EFFECTS ON SCRIPT RUNS - SEE NEWS MESSAGE <<<  
 'BIX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

=> d que 186

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L81      16 SEA FILE=WPIX ABB=ON  PLU=ON  P21/BIX (L) SIGNAL TRANSDUCT?/BIX
L82      39 SEA FILE=WPIX ABB=ON  PLU=ON  P21/BIX (L) PROTEIN KINAS?/BIX
L83      951 SEA FILE=WPIX ABB=ON  PLU=ON  (P21/BIX OR P 21/BIX)
L84      22202 SEA FILE=WPIX ABB=ON  PLU=ON  (WRINKL?/BIX OR SKIN WRINKL?/BIX
          OR WRINK? REDUC?/BIX OR SKIN AGING/BIX OR SKIN AGEING/BIX OR
          PHOTO/BIX (L) (AGING/BIX OR AGEING/BIX))
L86      2 SEA FILE=WPIX ABB=ON  PLU=ON  (L81 OR L82 OR L83) AND L84

```

=> s 186 not 185



L108 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1990:240313 CAPLUS  
 DOCUMENT NUMBER: 112:240313  
 TITLE: Cosmetic skin preparations containing nicorandil  
 INVENTOR(S): Nakayama, Taiichi; Fujii, Seishiro;  
 Kitamura, Kenji  
 PATENT ASSIGNEE(S): Shiseido Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE     |
|------------------------|------|----------|-----------------|----------|
| JP 02032006            | A2   | 19900201 | JP 1988-180228  | 19880721 |
| PRIORITY APPLN. INFO.: |      |          | JP 1988-180228  | 19880721 |

ED Entered STN: 23 Jun 1990  
 AB Skin preps. contain N-(2-hydroxyethyl)nicotinamide nitrate ester (I) or its salts as an active ingredient. The preps. prevent aging of the skin and damages caused by suntan, razors, etc. Glycerin 4.0, 1,3-butylene glycol 4.0, EtOH 7.0, poly(oxyethylene) oleyl ether 0.5, I 0.01, and H2O to 100% by weight to give a shaving lotion.  
 IC ICM A61K007-00  
 ICS A61K007-15; A61K031-44  
 CC 62-4 (Essential Oils and Cosmetics)  
 IT 65141-46-0, Nicorandil  
 RL: BIOL (Biological study)  
 (cosmetic skin preps. containing, for prevention of aging and damaging)

=> □

=> file medline

FILE 'MEDLINE' ENTERED AT 16:51:32 ON 28 APR 2006

FILE LAST UPDATED: 27 APR 2006 (20060427/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).  
 See also:

<http://www.nlm.nih.gov/mesh/>  
[http://www.nlm.nih.gov/pubs/techbull/nd04/nd04\\_mesh.html](http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html)  
[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_med\\_data\\_changes.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html)  
[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_2006\\_MeSH.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html)

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

halo, lower alkoxy) or II (R2-3 = H, alkyl). I and II have strong retinoic acid-like effects and show reduced cytotoxicity due to rapid in vivo metabolism, and are useful for prevention of **skin** damages from sunlight and **aging**. I (R1 = H) (III), prepared from 3-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2-propenoic acid and 4-HOC6H4CO2H, enhanced EGF-dependent proliferation of fibroblast and also showed other **skin** damage-protecting effects. A cosmetic lotion containing III was formulated.

- IC ICM A61K007-48  
ICS A61K007-00; A61K031-215; C07C069-608
- CC 62-4 (Essential Oils and Cosmetics)  
Section cross-reference(s): 1, 63
- IT **Aging**  
Cosmetics  
**Skin**, disease  
Sunscreens  
(**skin** preps. containing retinoids for prevention of **skin** damage from sunburn and **aging**)
- IT Retinoids  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(**skin** preps. containing retinoids for prevention of **skin** damage from sunburn and **aging**)
- IT Pharmaceutical dosage forms  
(topical, **skin** preps. containing retinoids for prevention of **skin** damage from sunburn and **aging**)
- IT 99-96-7, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(esterification with cyclohexenylpropenoic acid derivative; **skin** preps. containing retinoids for prevention of **skin** damage from sunburn and **aging**)
- IT 4951-39-7, 3-(2,6,6-Trimethyl-1-cyclohexen-1-yl)-2-propenoic acid  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(esterification with hydroxybenzoic acid; **skin** preps. containing retinoids for prevention of **skin** damage from sunburn and **aging**)
- IT 22824-31-3, 5,6,7,8-Tetrahydro-5,5,8,8-tetramethyl-2-naphthol  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(esterification with muconic acid; **skin** preps. containing retinoids for prevention of **skin** damage from sunburn and **aging**)
- IT 505-70-4, 2,4-Hexadienedioic acid  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(esterification with tetrahydronaphthol derivative; **skin** preps. containing retinoids for prevention of **skin** damage from sunburn and **aging**)
- IT 153233-07-9P  
RL: PNU (Preparation, unclassified); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)  
(selective hydrolysis of; **skin** preps. containing retinoids for prevention of **skin** damage from sunburn and **aging**)
- IT 153233-08-0P 153233-09-1P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(**skin** preps. containing retinoids for prevention of **skin** damage from sunburn and **aging**)

synthase inhibitors to prevent and reduce wrinkles. L-NAME treated mice show a reduction in fine wrinkles compared to untreated control mice which can prevent the formation of wrinkles caused by UVB exposure.

IC ICM A61K007-00

ICS A61K007-42; A61K007-44; A61K031-495

CC 62-4 (Essential Oils and Cosmetics)

Section cross-reference(s): 63

IT Skin, disease

(aging; NOS inhibitors for treatment of wrinkles)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L108 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:677661 CAPLUS

DOCUMENT NUMBER: 123:92914

TITLE: Preparation of retinoids for preventing skin damages and skin preparations containing them

INVENTOR(S): Ehama, Ritsuko; Sakamoto, Okihiko; Horii, Izumi; Akima, Kazuo; Fujii, Seishiro; Shudo, Koichi

PATENT ASSIGNEE(S): Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.

CODEN: JKXXAF

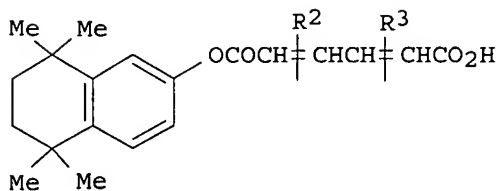
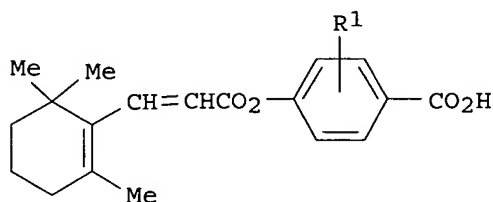
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.                  | KIND | DATE     | APPLICATION NO.  | DATE     |
|-----------------------------|------|----------|------------------|----------|
| JP 07118134                 | A2   | 19950509 | JP 1992-125625   | 19920417 |
| PRIORITY APPLN. INFO.:      |      |          | JP 1992-125625   | 19920417 |
| OTHER SOURCE(S):            |      |          | MARPAT 123:92914 |          |
| ED Entered STN: 15 Jul 1995 |      |          |                  |          |
| GI                          |      |          |                  |          |



AB The skin preps. contain retinoids I (R1 = H, lower alkyl, OH,

WO 2005123010 A1 20051229 WO 2005-US20666 20050610  
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,  
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,  
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,  
 LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,  
 NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,  
 SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,  
 ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,  
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,  
 EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,  
 RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,  
 MR, NE, SN, TD, TG

## PRIORITY APPLN. INFO.:

US 2004-578799P

P 20040610

ED Entered STN: 15 Dec 2005

AB Disclosed is, inter alia, a method of reducing UVB-induced wrinkles in a subject, the method that includes: administering to a subject having, or at risk for, UVB-induced wrinkle, a composition comprising an agent that inhibits ATR mediated signaling. Thus, topical 1.2% caffeine in acetone was prepared and applied on the back of UVB irradiated and non-UVB irradiated mice. Caffeine was effective in reducing UVB-induced wrinkle formation.

IC ICM A61K007-42

ICS A61K031-522

INCL 424059000; 514263340

CC 62-4 (Essential Oils and Cosmetics)

IT Skin, disease

(aging, wrinkles, inhibition of; topical caffeine for  
 inhibition of ATR mediated signaling for reducing UVB-induced wrinkles)

L108 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:615365 CAPLUS

DOCUMENT NUMBER: 137:159039

TITLE: NOS inhibitors for treatment of wrinkles

INVENTOR(S): Fujii, Seishiro; Lerner, Ethan

PATENT ASSIGNEE(S): The General Hospital Corporation, USA

SOURCE: PCT Int. Appl., 15 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| WO 2002062306   | A1   | 20020815 | WO 2002-US2292  | 20020125 |
| W: JP   |      |          |                 |          |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR    |      |          |                 |          |
| US 2002168325   | A1   | 20021114 | US 2002-57247   | 20020125 |
| EP 1359885  | A1   | 20031112 | EP 2002-720854  | 20020125 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR |      |          |                 |          |
| JP 2004520388   | T2   | 20040708 | JP 2002-562314  | 20020125 |
| US 2003207844   | A1   | 20031106 | US 2003-406306  | 20030403 |

## PRIORITY APPLN. INFO.:

US 2001-264176P

P 20010125

US 2002-57247

A3 20020125

WO 2002-US2292

W 20020125

ED Entered STN: 16 Aug 2002

AB Methods, compns., and kits, are provided for the use of nitric oxide

SOURCE: Foundation of the University of Central Florida  
 PCT Int. Appl., 36 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE       |
|--|------|----------|-----------------|------------|
| WO 2005077019  | A2   | 20050825 | WO 2005-US3908  | 20050207   |
| WO 2005077019  | A3   | 20060216 |                 |            |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,<br>CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,<br>GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,<br>LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,<br>NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,<br>TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM<br>RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,<br>AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,<br>EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,<br>RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,<br>MR, NE, SN, TD, TG |      |          |                 |            |
| US 2005250799  | A1   | 20051110 | US 2005-52149   | 20050207   |
| PRIORITY APPLN. INFO.:   |      |          | US 2004-542187P | P 20040205 |

OTHER SOURCE(S): MARPAT 143:234993

ED Entered STN: 26 Aug 2005

AB Methods, compns., and kits are provided for the use of inhibitors of  
 protease, i.e., caspase or serine protease involved in apoptosis to reduce  
 wrinkles or other skin damage caused by exposure to UVB radiation. The  
 protease inhibitor is administered, e.g., topically in a cosmetic or  
 therapeutic composition. Thus, UCF-101, an Omi/HtrA2 serine protease inhibitor  
 was non-irritating to UVB-exposed skin in mice. Inhibition of Omi/HtrA2  
 serine protease by 1% UCF-101 in DMSO was effective at preventing and  
 reducing UVB-induced wrinkle formation in mice. It was also effective at  
 reducing UVB-induced dilation of blood vessels.

IC ICM A61K

CC 62-4 (Essential Oils and Cosmetics)

Section cross-reference(s): 1, 63

IT **Skin**, disease

(aging; topical compns. containing protease inhibitors for  
 treatment of UVB-induced **skin** damage and wrinkles)

L108 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1308526 CAPLUS

DOCUMENT NUMBER: 144:40401

TITLE: Topical caffeine for inhibition of ATR mediated  
 signaling for reducing UVB-induced wrinkles

INVENTOR(S): Nghiem, Paul; **Fujii, Seishiro**

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 13 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| US 2005276765 | A1   | 20051215 | US 2005-149126  | 20050609 |

D05-H09; D05-H12A; D05-H12D5; D05-H14B2; D05-H17A6; D05-H18; D09-E01  
AN 2004-295301 [27] WPIX  
AB WO2004026249 A UPAB: 20040426

NOVELTY - Screening of **wrinkles reducing agent** involves determination of the test agent to increase or induces a component (C1) of the **p21 signal transduction** pathway and correlating the ability of the test agent to increase expression, activity or levels of (C1) with the agent's ability to reduce the appearance or formation of **wrinkles**.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

- (a) a cosmetic composition comprising an agent that increases or induces **p21**;
- (b) providing a record involves determination of the test agent to increase or induces **p21**;
- (c) generating the record that correlates the ability of the test agent; and
- (d) a kit comprises a composition comprising an agent that increases or induces (C1); and instructions for using the composition.

ACTIVITY - Dermatological.

MECHANISM OF ACTION - None given.

USE - As a cosmetic for preventing or treating **wrinkles**, for reducing the appearance or formation of **wrinkles** on the skin (claimed) and in the manufacture of medicament for preventing skin damage e.g. UVB-induce skin damage.

ADVANTAGE - The **p21 signal transduction** pathway prevents skin damage, reduces the appearance or formation of **wrinkles** on the skin and UVB-induce skin damage.  
Dwg.0/0

TECH UPTX: 20040426  
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: The method further involving evaluating the effect of the agent on UVB-induced **wrinkles** on the skin of a subject and selecting the test agent that increases expression, activity or levels of (C1). Determination involves providing a cell, tissue or non-human subject comprising an exogenous nucleic acid comprising a regulatory region of (C1) operably linked to a nucleotide sequence encoding a reporter polypeptide and evaluating the ability of the test agent to increase the activity of the reporter polypeptide in the cell, tissue or non-human subject. The test agent is determined to increase or induce (C1) if it increases the activity of the reporter polypeptide.  
Preferred Composition: The composition further comprises a cosmetic ingredient.  
Preferred Components: The cosmetic ingredient is fragrance or sunscreen.  
The component of the **p21 signal transduction** pathway is **p21**.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Components: The test agent is animal extract, botanical extract, fungal extract, small molecule, protein, lipid or nucleic acid.

L108 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2005:902724 CAPLUS  
DOCUMENT NUMBER: 143:234993  
TITLE: Protease inhibitors for treatment of wrinkles  
INVENTOR(S): Fujii, Seishiro; Hirakawa, Satoshi; Detmar, Michael; Zervos, Antonis S.  
PATENT ASSIGNEE(S): The General Hospital Corporation, USA; Research